Tunga Turthi
10/731759

FILE 'REGISTRY' ENTERED AT 12:40:02 ON 17 JAN 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 JAN 2006 HIGHEST RN 871978-73-3
DICTIONARY FILE UPDATES: 15 JAN 2006 HIGHEST RN 871978-73-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

```
                E POLYMETHYLENE/CN 5
                E POLYETHYLENE/CN 5
L1            1 S E3
                E POLYBUTYLENE/CN 5
L2            1 S E3
                E POLYPROPYLENE/CN 5
L3            1 S E3
                E POLYOXYMETHYLENE/CN 5
                E POLYOXYETHYLENE/CN 5
                E POLYOXYBUTYLENE/CN 5
                E POLYOXYPROPYLENE/CN 5
                E POLYETHYLENE GLYCOL/CN 5
L4            1 S E3
                E POLYPROPYLENE GLYCOL/CN 5
L5            1 S E3
                E POLYVINYL ALCOHOL/CN 5
                E METHOXYPOLYETHYLENE GLYCOL/CN 5
                E "METHOXY(POLYETHYLENE GLYCOL)"/CN 5
                E "METHOXY (POLYETHYLENE GLYCOL)"/CN 5
L6            1 S 9004-74-4/RN
                E "METHOXYPOLY(ETHYLENE GLYCOL)"/CN 5
L7            1 S E3
```

Searcher : Shears 571-272-2528

```
L8              6 S L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7


                  E CYSTEINE/CN 5
L14             2 S E3


                  E POLYVINYL ALCOHOL/CN 5
                  E "POLY(VINYL ALCOHOL)"/CN 5
L17             1 S E3

FILE 'HCAPLUS' ENTERED AT 12:40:02 ON 17 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 17 Jan 2006  VOL 144 ISS 4
FILE LAST UPDATED: 16 Jan 2006  (20060116/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L1              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYETHYLENE/CN
L2              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYBUTYLENE/CN
L3              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYPROPYLENE/CN
L4              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "POLYETHYLENE GLYCOL"/CN

L5              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "POLYPROPYLENE GLYCOL"/CN

L6              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  9004-74-4/RN
L7              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "METHOXYPOLY(ETHYLENE
                  GLYCOL)"/CN
L8              6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR
                  L5 OR L6 OR L7
L9         461491 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR POLYALKYLENE OR
                  POLYALKENYLENE OR POLYOXYALKYLENE OR POLY(W)(ALKYLENE OR
                  ALKENYLENE OR OXYALKYLENE OR OXY ALKYLENE OR METHYLENE OR
                  PROPYLENE OR ETHYLENE OR BUTYLENE) OR POLYOXY ALKYLENE
L10        505667 SEA FILE=HCAPLUS ABB=ON  PLU=ON  POLY(W)(OXYMETHYLENE OR
                  OXYETHYLENE OR OXYBUTYLENE OR OXYPROPYLENE) OR POLYOXYMETHY
                  LENE OR POLYOXYETHYLENE OR POLYOXYBUTYLENE OR POLYOXYPROPYL
                  ENE OR POLYETHYLENE OR POLYBUTYLENE OR POLYMETHYLENE OR
                  POLYETHYLENE OR POLYSACCHARIDE OR POLY SACCHARIDE OR PEG
L11        235187 SEA FILE=HCAPLUS ABB=ON  PLU=ON  POLYPROPYLENE OR (POLYVINY
                  L OR POLY VINYL)(W)(ALC OR ALCOHOL) OR METHOXYPOLYETHYLENE
L14             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYSTEINE/CN
```

L17 1 SEA FILE=REGISTRY ABB=ON PLU=ON "POLY(VINYL ALCOHOL)"/CN

L18 12264 SEA FILE=HCAPLUS ABB=ON PLU=ON (L9 OR L10 OR L11 OR L17 OR PVA OR PPG OR MPEG) AND ANTIBOD?

L19 389 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 AND (VL OR VH OR HEAVY OR LIGHT OR V(2W)(H OR L))(5A)CHAIN

L20 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND (L14 OR CYS OR CYSTEIN##)

L37 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 NOT (PY=>1996 OR PD=>19961210) ← Restrict to only cites dated prior to 12-10-96

L37 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 04 Jan 1996
ACCESSION NUMBER: 1996:7216 HCAPLUS
DOCUMENT NUMBER: 124:84379
TITLE: Thermal stabilization of a single-chain Fv **antibody** fragment by introduction of a disulfide bond
AUTHOR(S): Young, N. Martin; MacKenzie, C. Roger; Narang, Saran A.; Oomen, Raymond P.; Baenziger, John E.
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, 100 Sussex Drive, Ottawa, ON, K1A 0R6, Can.
SOURCE: FEBS Letters (1995), 377(2), 135-9
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A disulfide bond was introduced into a single-chain Fv form of the anti-carbohydrate **antibody**, Se155-4 by replacing Ala-L57 of the **light chain** and Asp-H106 of the **heavy chain** with **cysteines**, by site-directed mutagenesis. To maintain the salt-bridge from the latter residue to Arg-H98, Tyr-107 was also altered to Asp. The resulting ds-scFv was shown to retain full antigen-binding activity, by enzyme immunoassay and surface plasmon resonance anal. of binding kinetics. Compared with the parent scFv, the disulfide bonded form was shown to have enhanced thermal stability, by Fourier transform IR spectroscopy. The Tm was raised from 60° to 69°. The ds-scFv form thus combines the stable monomeric form of the disulfide form with the expression advantages of the scFv.

L37 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 22 Nov 1995
ACCESSION NUMBER: 1995:934393 HCAPLUS
DOCUMENT NUMBER: 124:15376
TITLE: A novel strategy affords high-yield coupling of **antibody** Fab' fragments to liposomes
AUTHOR(S): Shahinian, Serge; Silvius, John R.
CORPORATE SOURCE: Department of Biochemistry, McGill University, Montreal, QC, H3G 1Y6, Can.
SOURCE: Biochimica et Biophysica Acta, Biomembranes (1995), 1239(2), 157-67
CODEN: BBBMBS; ISSN: 0005-2736
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new assay for the production of reactive sulfhydryl-bearing **antibody** Fab' fragments has been utilized to develop

conditions affording high efficiencies of coupling of mouse and rabbit IgG-derived Fab' fragments to lipid vesicles containing maleimidyl-functionalized phospholipids. **Cysteine** and mercaptoethylamine, but not dithiothreitol, reduce **antibody** F(ab')2 to Fab' fragments in very good yields under conditions where overredn. to **heavy** and **light chains** is minimized. Surprisingly, however, a large fraction of the Fab' fragments generated under these conditions can lack maleimide-reactive sulfhydryl groups, as demonstrated using a maleimidyl-**poly(ethylene** glycol) conjugate to shift selectively the electrophoretic mobility of the reactive sulfhydryl-bearing Fab' fragments. After modification of F(ab')2 reduction conditions specifically to maximize the yield of the latter fraction, it is possible to achieve high and very reproducible coupling of functional Fab' fragments to liposomes (equivalent to coupling of ca. 70% of total input protein and almost 100% of the reactive sulfhydryl-bearing Fab' fraction). A novel phospholipid-**poly(ethylene** glycol)-maleimide 'anchor' allows particularly efficient coupling of Fab' fragments to liposomes, even using relatively low liposome concns. and molar percentages of the liposome-incorporated 'anchor' species. These results demonstrate that with appropriate optimization of the conditions for Fab' production and liposome coupling, Fab' fragments can be coupled to liposomes with efficiencies comparable to or exceeding those reported for coupling of intact **antibodies** . These results should facilitate the wider use of Fab' fragments as a potentially advantageous alternative to intact **antibodies** for liposomal targeting in various applications.

IT **52-90-4**, L-**Cysteine**, biological studies
RL: BSU (Biological study, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(a novel strategy affords high-yield coupling of **antibody** Fab' fragments to liposomes)

L37 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1983:610916 HCAPLUS
DOCUMENT NUMBER: 99:210916
TITLE: A new isotype sequence (Vκ27) of the variable region of κ- **light chains** from a mouse hybridoma-derived anti-(streptococcal group A **polysaccharide**) **antibody** containing an additional **cysteine** residue. Application of the dimethylaminoazobenzene isothiocyanate technique for the isolation of peptides
AUTHOR(S): Chang, Jui Yoa; Herbst, Hermann; Aebersold, Ruedi; Braun, Dietmar G.
CORPORATE SOURCE: Pharm. Res. Lab., Ciba-Geigy Ltd., Basel, CH-4002, Switz.
SOURCE: Biochemical Journal (1983), 211(1), 173-80
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 1st complete sequence of the variable region of a κ- **light chain** (Vκ) from a mouse anti-(streptococcal group A **polysaccharide**) IgG3 **antibody** (Ig 7S34.1) is reported. Ig 7S34.1 was isolated from the ascitic fluid of mouse hybridoma 7S34.1, previously cloned in vitro. A recently developed technique for the isolation of peptides,

using precolumn formation of peptide derivs. with dimethylaminoazobenzene isothiocyanate, was used to determination the complete sequence. The sequence of the variable region of the κ-**light chain** of Ig 7S34.1 defines a new mouse Vκ isotype (Vκ27); this is the 1st mouse Ig **light** -**chain** variable region shown to have an extra **cysteine** residue at position 48.

L37 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1983:609061 HCAPLUS
DOCUMENT NUMBER: 99:209061
TITLE: A new method for the selective isolation of **cysteine**-containing peptides. Specific labeling of the thiol group with a hydrophobic chromophore
AUTHOR(S): Chang, Jui Yoa; Knecht, Rene; Braun, Dietmar G.
CORPORATE SOURCE: Pharm. Res. Lab., Ciba-Geigy Ltd., Basel, CH-4002, Switz.
SOURCE: Biochemical Journal (1983), 211(1), 163-71
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new method for the selective isolation of **cysteine**-containing peptides was designed which was based on the specific labeling of thiol groups with a hydrophobic chromophore followed by enzymic fragmentation of the labeled protein and reversed-phase high-pressure liquid-chromatog. separation of the peptide mixture Only **cysteine** -containing peptides are detected in the visible region with sensitivity at the low picomole level; this high sensitivity allows isolation of nanogram amts. of pure **cysteine**-containing peptide. During sequence determination of the chromophore-labeled **cysteine**-containing peptides, the **cysteine** residues are released as colored anilinothiazolinone derivs. and can be detected directly in the picomole range. With proteins bearing several disulfide groups, each disulfide group may undergo a different degree of reduction, and therefore the recovery of individual **cysteine**-containing peptides may be used to deduce the disulfide links present in the native protein. Two thiol-specific reagents, 4-methylaminoazobenzene 4'-iodoacetamide and 4-dimethylaminoazobenzene 4'-N-maleimide, were synthesized and characterized. The method was successfully used to isolate 5 **cysteine**-containing peptides from a completely reduced monoclonal-**antibody** κ- **light chain** raised against the azobenzenearsonate determinant and 6 **cysteine** -containing peptides from a κ- **light chain** raised against streptococcal group A **polysaccharide**. The principle of this method is applicable to the isolation of any peptide containing amino acid residues that can be specifically labeled with a hydrophobic chromophore.
IT **52-90-4D**, peptides containing
RL: ANST (Analytical study)
(separation of, by high-pressure liquid chromatog., hydrophobic chromophore labeling of thiol group in)

L37 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1980:547840 HCAPLUS
DOCUMENT NUMBER: 93:147840

TITLE: Isolation of an active **heavy-chain** variable domain from a homogeneous rabbit **antibody** by cathepsin B digestion of the aminoethylated **heavy chain**
AUTHOR(S): Ehrlich, Paul H.; Matsueda, Gary R.; Margolies, Michael N.; Husain, S. Shaukat; Haber, Edgar
CORPORATE SOURCE: Massachusetts Gen. Hosp., Harvard Med. Sch., Boston, MA, 02114, USA
SOURCE: Biochemistry (1980), 19(17), 4091-6
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsin B from bovine liver was used to cleave the **heavy chain** of partially reduced and aminoethylated rabbit allotype a1 IgG. Three major cleavages were identified, one of which appears to be at the peptide bond carboxy terminal to the two adjacent (aminoethyl)**cysteine** residues at positions 133 and 134. The variable domain of the **heavy chain** (**VH**) was isolated by gel filtration from both pooled heterogeneous rabbit IgG and a homogeneous rabbit antitype III pneumococcal **polysaccharide antibody**. This VH inhibited the binding of 125I-labeled (allotype a1) IgG to anti-a1 allotypic **antibodies**. The recombinant mol. consisting of **VH** and **light chain** from the homogeneous **antibody** is active in an antigen-binding assay.

L37 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1973:464350 HCAPLUS
DOCUMENT NUMBER: 79:64350
TITLE: Amino terminal sequence of **antibody light chains**. Evidence for possible inheritance of structural genes
AUTHOR(S): Braun, Dietmar G.; Jaton, Jean C.
CORPORATE SOURCE: Basel Inst. Immunol., Basel, Switz.
SOURCE: Immunochemistry (1973), 10(6), 387-95
CODEN: IMCHAZ; ISSN: 0019-2791
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Amino-terminal sequence analyses of 12 rabbit **antibody light chains** with restricted heterogeneity induced with either streptococcal group or pneumococcal type antigens are described. A comparison of their 27-30 N-terminal residue positions and comparison with the homologous regions of human and mouse κ chains suggest the following conclusions: Rabbit, mouse, and human κ chains are homologous. They share the prototype N-terminal sequence Asp-Ile-Val-Met-Thr-Gln and predominantly or exclusively a number of residues further on in the N-terminal 27 positions (e.g., Pro 9, Gly 17, Thr 21, Ile 22, **Cys** 24, Ala 26, and Ser 27). The prototype rabbit **light chain** sequence appears to start with Ala-Asp-Ile-Val-Met, and is thus longer by 1 residue than human and mouse κ chains. Like their human and mouse counterparts, rabbit κ chains can be subgrouped. A min. number of 6 subgroups is distinguishable on the basis of the current sequence information. The existence of species-specific amino acid residues in the region reported appears to be doubtful because positions 12 and 18 are also variable. Rabbit allotype b4 **light chains** show the greatest variations in the N-terminal 5 amino acid positions,

with the highest variability index in position 3. The degree of homol. of **antibody light chain** N-termini appears to be a function of the breeding relation of individual rabbits. For example, **antibody light chains** of a parent and an offspring rabbit with identical specificities were identical within their N-terminal 22 amino acid residues. These data would imply inheritance of structural v-region genes for the synthesis of specific anti-**polysaccharide antibodies**.

L37 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1972:430629 HCAPLUS
DOCUMENT NUMBER: 77:30629
TITLE: Obtaining large variable-region peptides from rabbit **light chains**
AUTHOR(S): Freedlender, Elizabeth F.; Haber, Edgar
CORPORATE SOURCE: Dep. Med., Harvard Med. Sch., Boston, MA, USA
SOURCE: Biochemistry (1972), 11(12), 2362-70
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method for the isolation of large variable regions of rabbit **light chain** was developed. **Light chains** were isolated from an antipneumococcal **polysaccharide antibody** of restricted heterogeneity from a single rabbit homozygous for the b4 **light-chain** allotype. Disc gel electrophoresis indicated that the **antibody** preparation contained 4 distinguishable electrophoretic species of **light chain**. After complete reduction and alkylation with 14C-labeled iodoacetic acid to label the **cysteines** involved in the intrachain disulfide bonds, the **light chains** were maleylated and digested with trypsin. Gel filtration separated the digest into a fraction containing the constant region, 2 containing variable-region peptides and one containing the carboxyl-terminal tripeptide. Ion-exchange chromatog. resolved the major fraction containing variable-region peptides into the amino-terminal peptides and 2 other variable-region peptides. The amino-terminal peptides of .apprx.50 residues were isolated as a single fraction. The **antibody** derived peptides had amino-terminal sequences identical with those of the original **light-chain** preparation Peptide maps of the chymotryptic digest of this fraction indicated that several constant region peptides were missing and the amino acid composition was different from that of whole **light chain**. Two other variable-region peptides of .apprx.65 residues were isolated using the same procedure. One of these had Phe-Ser-Gly-Ser-Gly as its amino-terminal sequence. This sequence is characteristic of all k **light chains** and occurs following Arg-62. The other peptide had an amino-terminal sequence which could not be placed by homology with any of the reported mouse or human sequences. Peptide maps suggested that these 2 peptides included homologous stretches and continued into the constant region. The **antibody light chain** used as starting material contained several sequences as evidenced by more than one amino acid released at each step of the Edman degradation. In the amino-terminal peptide fraction isolated after limited cleavage, the same residues were again present. This indicates that the amino-terminal peptides of all the chains initially present were

not separated from each other, although they were separated from nonamino-terminal peptides. This suggests that the method should be generally applicable to isolating the homologous peptides from any rabbit **antibody**.

L37 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1970:485858 HCAPLUS
DOCUMENT NUMBER: 73:85858
TITLE: Isolation and characterization of structurally homogeneous **antibodies** from antipneumococcal sera
AUTHOR(S): Jaton, Jean C.; Waterfield, Michael D.; Margolies, Michael N.; Haber, Edgar
CORPORATE SOURCE: Harvard Med. Sch., Massachusetts Gen. Hosp., Boston, MA, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1970), 66(3), 959-66
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Antibodies** of sufficient homogeneity for sequence studies were readily obtained in high concns. from rabbits immunized with pneumococcal vaccines. By taking advantage of slightly differing immunol. specificity for type III and type VIII capsular **polysaccharides**, an **antibody** with unique electrophoretic mobility could be isolated from serum containing several distinct **antibody** components by using appropriate cross-reacting immunoadsorbents. A unique sequence for the N-terminal 11 amino acid residues of the **light chain** of the **antibody** was found, in contrast to several sequences in the **antibody** mixture from which this component was isolated. The sequence of a nonimmune **light chain** pool demonstrated even greater heterogeneity. Chymotryptic peptide maps of the **antibody light chain** showed 2 unique **cysteine**-containing variable-region peptides not seen in maps of nonimmune **light chain** pools of the same allotypic specificity as that of the **antibody light chain**. The exptl. approach described may provide further insight into the structure-function relation of several homogeneous **antibodies** of closely related specificity for the same **polysaccharide** antigen.

FILE 'MEDLINE' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'BIOSIS' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'EMBASE' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'WPIDS' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'CONFSCI' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'SCISEARCH' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'JICST-EPLUS' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'JAPIO' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'RAPRA' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'PROMT' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'PASCAL' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'CBNB' ENTERED AT 12:40:46 ON 17 JAN 2006

FILE 'CIN' ENTERED AT 12:40:46 ON 17 JAN 2006

L38 47 S L20
L39 39 DUP REM L38 (8 DUPLICATES REMOVED)

L39 ANSWER 1 OF 39 WPIDS
ACCESSION NUMBER: 2005-417682 [42] WPIDS
DOC. NO. CPI: C2005-127965
TITLE: New polypeptides that bind low density lipoprotein and its oxidized forms, useful as antilipemic agents and for treating kidney disease, are human monoclonal **antibodies.**
DERWENT CLASS: B04 D16
INVENTOR(S): MUELLER-HERMELINK, H K; VOLLMERS, H; VOLLMERS, P
PATENT ASSIGNEE(S): (MUEL-I) MUELLER-HERMELINK H K; (VOLL-I) VOLLMERS H; (VOLL-I) VOLLMERS P
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005049635	A2	20050602	(200542)*	GE	42

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

DE 10353175	A1	20050616	(200542)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005049635	A2	WO 2004-DE2503	20041112
DE 10353175	A1	DE 2003-10353175	20031114

PRIORITY APPLN. INFO: DE 2003-10353175 20031114
AN 2005-417682 [42] WPIDS
AB WO2005049635 A UPAB: 20050704
NOVELTY - Purified polypeptides (I) are new. They have an amino acid (aa) sequence practically identical with sequences (1; 96 aa) and/or (3; 110 aa), reproduced, and bind to low density lipoprotein (LDL), especially LDL-cholesterol, and/or their oxidized forms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) purified polypeptides that include sequences (1) and/or (3);

(2) complementarity determining regions (CDR), or their functional fragments, of (1) and/or (3); and

(3) method for generating **antibodies** (Ab) by the hybridoma technique in which hybridomas are prepared from the heteromyeloma cell line HAB-1, or its subclones, and B lymphocytes from human spleen, lymph nodes or blood.

ACTIVITY - Antilipemic; Nephrotropic; Antiarteriosclerotic; Cardiant. Purified SAM-6.10 **antibody** (containing (1) and (3) as its variable regions) was injected (1 mg) intraperitoneally into mice, then the LDL content in the serum determined. The contents were 14 and 12 mg/dl after 24 and 48 hours, respectively; contrast 18 and 17 for an animal injected with 1 mg of an isotype control **antibody**.

MECHANISM OF ACTION - Binding to (oxidized) low density lipoprotein, so functioning in a manner analogous to the known scavenger pathway.

USE - (I) are useful:

(i) as hypolipemic agents, for reducing the level of (oxidized) low density lipoprotein, especially cholesterol, in the blood, e.g. for treating arteriosclerosis and its sequelae such as cardiac infarct; and

(ii) for treating kidney disease, particularly glomerulonecrosis.

ADVANTAGE - (I) avoid the side effects associated with use of inhibitors of key enzymes in cholesterol biosynthesis.

Dwg.0/7

L39 ANSWER 2 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-101475 [11] WPIDS
CROSS REFERENCE: 2005-081945 [09]
DOC. NO. CPI: C2005-033920
TITLE: New modified **antibody** Fab' or Fab fragments to which two or more effector molecules are attached, useful for modulating protein protein interactions or for diagnosing or treating e.g. infection, inflammation, cancer or diabetes.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): HEYWOOD, S P; HUMPHREYS, D P
PATENT ASSIGNEE(S): (CLLT) CELLTECH R & D LTD
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2005003171 A2 20050113 (200511)* EN 39
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005003171	A2	WO 2004-GB2871	20040701

PRIORITY APPLN. INFO: GB 2003-15457 20030701
AN 2005-101475 [11] WPIDS
CR 2005-081945 [09]
AB WO2005003171 A UPAB: 20050217
NOVELTY - An **antibody** Fab' or Fab fragment to which two or more effector molecules are attached, is new.
DETAILED DESCRIPTION - The **antibody** Fab' or Fab fragment is characterized in that:
(a) the interchain **cysteine** of CH1 or CL has been replaced by another amino acid; or
(b) both the interchain **cysteine** of CH1 and CL have been replaced by another amino acid and an engineered **cysteine** in the **light chain** constant region is covalently bonded to a **cysteine** in the hinge region.
INDEPENDENT CLAIMS are also included for:
(1) producing the above **antibody** Fab' or Fab fragment;
(2) a host cell expressing the **antibody** fragment; and
(3) a pharmaceutical composition comprising the above **antibody** fragment together with one or more pharmaceutical excipients, diluents or carriers.
ACTIVITY - Antimicrobial; Antiinflammatory; Cytostatic; Antiasthmatic; Antipsoriatic; Neuroprotective; Immunosuppressive; Antidiabetic. No biological data given.
MECHANISM OF ACTION - Gene Therapy.
USE - The composition and methods are useful for various diagnostic and therapeutic applications, particularly for modulating protein:protein interactions. These may be used for diagnosing or treating diseases such as infection, inflammation, cancer, asthma, psoriasis, neurologic diseases, organ-transplant rejection or diabetes.
Dwg.0/7

L39 ANSWER 3 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-081946 [09] WPIDS
DOC. NO. CPI: C2005-028552
TITLE: Novel **antibody** Fab/Fab' fragment attached with effector molecule, in which **heavy chain** in fragment not bonded to **light chain**, and interchain **cysteine** of CL and CH1 replaced with another amino acid, useful for treating fungal infection.
DERWENT CLASS: B04 D16

INVENTOR(S): CARRINGTON, B; HEYWOOD, S P; HUMPHREYS, D P
PATENT ASSIGNEE(S): (CLLT) CELLTECH R & D LTD
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005003170	A2	20050113	(200509)*	EN	40

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005003170	A2	WO 2004-GB2870	20040701

PRIORITY APPLN. INFO: GB 2003-15450 20030701
AN 2005-081946 [09] WPIDS
AB WO2005003170 A UPAB: 20050207
NOVELTY - An **antibody** Fab or Fab' fragment (I) to which one or more effector molecule being attached, where the **heavy chain** in the fragment not covalently bonded to the **light chain** and both the interchain **cysteine** of CL and the interchain **cysteine** of CH1 replaced with another amino acid, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) producing (I);
(2) a mixture (II) containing two or more Fab or Fab' fragments, where (II) is enriched for Fab or Fab' fragments in which the **light chain** in the fragments is not covalently bonded to the **heavy chain**, both the interchain **cysteines** of CL and CH1 have been replaced by another amino acid and one or more effector molecule is attached to the fragment; and
(3) a pharmaceutical composition comprising (I) or (II), together with one or more excipients, diluents or carriers.

ACTIVITY - Antibacterial; Fungicide; Antiinflammatory; Immunosuppressive; Antirheumatic; Antiarthritic; Gastrointestinal-Gen.; Cytostatic; Antiallergic; Antiasthmatic; Dermatological; CNS-Gen.; Respiratory-Gen.; Antipsoriatic; Neuroprotective; Antidiabetic.

In vivo analysis of the efficacy of the **antibody** g8516 Fab'-**polyethylene** glycol (**PEG**) in neutralizing antigen (interleukin) (IL) was carried out as follows. Male Balb/c mice (19.9 g) were injected intravenously with the **antibody** at 1, 3 and 10 mg/kg in phosphate buffered saline (PBS) (100 micro l), or PBS vehicle alone. The mice were injected with the antigen (human IL-1 beta) (30 micro g/kg) in PBS vehicle (100 micro l) or PBS. Cardiac puncture was performed and blood was collected. Plasma was prepared from the sampled blood by centrifugation and subjected to determination of IL levels by enzyme linked immunosorbent assay (ELISA). The result indicated neutralization of IL in the mice treated

with the **antibody**, when compared with the mice administered with PBS.

MECHANISM OF ACTION - Immune stimulator; Neutralizes antigen-induced IL-6 generation.

USE - (I) is useful in the detection or treatment of diseases or disorders, including bacterial infection, fungal infection, inflammatory disease/autoimmunity e.g., rheumatoid arthritis and inflammatory bowel disease, cancer, allergic/atopic disease e.g., asthma and eczema, congenital disease e.g., cystic fibrosis, and psoriasis, multiple sclerosis and diabetes. (I) is useful for neutralizing medically relevant antigen such as those antigens upregulated during disease or infection, for e.g., soluble antigens such as interleukins.

Dwg.0/12

L39 ANSWER 4 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-081945 [09] WPIDS
CROSS REFERENCE: 2005-101475 [11]
DOC. NO. CPI: C2005-028551
TITLE: **Antibody** Fab fragment useful in detection or treatment of diseases such as infectious disease, rheumatoid arthritis, cancer, asthma and diabetes, comprises **heavy chain** constant region terminating at interchain **cysteine** of CH1.
DERWENT CLASS: B04 D16
INVENTOR(S): HEYWOOD, S P; HUMPHREYS, D P
PATENT ASSIGNEE(S): (CLLT) CELLTECH R & D LTD
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005003169	A2	20050113	(200509)*	EN	30

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005003169	A2	WO 2004-GB2810	20040701

PRIORITY APPLN. INFO: GB 2003-19588 20030820; GB 2003-15457 20030701

AN 2005-081945 [09] WPIDS
CR 2005-101475 [11]
AB WO2005003169 A UPAB: 20050217

NOVELTY - An **antibody** Fab fragment (I) comprising the **heavy chain** constant region terminating at the interchain **cysteine** of CH1, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) producing (M1) an **antibody** Fab fragment having one or more effector molecules attached to it comprising treating (I) with a reducing agent capable of generating a free thiol group in a **cysteine** of the **heavy** and **light chain** constant region, and reacting the treated fragment with an effector molecule;

(2) a mixture (II) containing two or more **antibody** Fab fragments, the mixture being enriched for Fab fragments in which the CH1 domain terminates at the interchain **cysteine**, the **heavy chains** in the fragments are not covalently bonded to the **light chains** and the fragments have an effector molecule attached to a **cysteine** in the **light chain** and the **heavy chain** constant region;

(3) an isolated DNA sequence (III) encoding the **heavy** and/or **light chain** constant regions of (I);

(4) a cloning or expression vector (IV) comprising one or more of (III);

(5) a host cell (V) expressing (I);

(6) preparation of (I); and

(7) a pharmaceutical composition comprising (I), together with one or more excipients, diluents or carriers.

ACTIVITY - Antimicrobial; Antibacterial; Fungicide; Antiinflammatory; Antiarthritic; Antirheumatic; Antipsoriatic; Osteopathic; Gastrointestinal-Gen.; Cytostatic; Antiallergic; Dermatological; Neuroprotective; Immunosuppressive; Antidiabetic; Antiasthmatic; CNS-Gen.; Respiratory-Gen.; Antianemic; Antisickling.

No biological data given.

MECHANISM OF ACTION - Immunotherapy.

USE - (I) is useful in the detection or treatment of number of diseases or disorders such as infectious disease e.g., bacterial infection, fungal infection; inflammatory disease/autoimmunity e.g., rheumatoid arthritis, osteo arthritis, inflammatory bowel disease; cancer; allergic/atopic disease e.g., asthma, eczema, congenital disease e.g., cystic fibrosis, sickle cell anemia; dermatological disease e.g., psoriasis; neurological disease e.g., multiple sclerosis; transplants e.g., organ transplant rejection, graft-versus-host disease; and metabolic/idiopathic disease e.g., diabetes.

ADVANTAGE - (I) avoids the need to engineer modified hinge regions and/or surface amino acid substitutions, which are required for site-specific effector molecule attachment. (I) can be attached easily and efficiently at low cost.

Dwg.0/5

L39 ANSWER 5 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER:	2005-365630 [37] WPIDS
DOC. NO. NON-CPI:	N2005-296380
DOC. NO. CPI:	C2005-112376
TITLE:	Novel binding protein having Ig constant or variable heavy and light regions, or antigen binding domain capable of binding to human interleukin-18, useful for treating disorder associated with detrimental IL-18 activity e.g. cancer.
DERWENT CLASS:	A89 B04 D16 S03
INVENTOR(S):	BABCOOK, J; GHAYUR, T; GREEN, L; HEDBERG, B; JIA, X; KANG, J S; LABKOVSKY, B; VOSS, J W; WIELER, J
PATENT ASSIGNEE(S):	(BABC-I) BABCOOK J; (GHAY-I) GHAYUR T; (GREE-I) GREEN L; (HEDB-I) HEDBERG B; (JIAX-I) JIA X; (KANG-I) KANG

J S; (LABK-I) LABKOVSKY B; (VOSS-I) VOSS J W;
(WIEL-I) WIELER J; (ABBO) ABBOTT LAB

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005100965	A1	20050512	(200537)*		87
WO 2005047307	A2	20050526	(200537)	EN	

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005100965	A1	US 2003-706689	20031112
WO 2005047307	A2	WO 2004-US37971	20041112

PRIORITY APPLN. INFO: US 2003-706689 20031112

AN 2005-365630 [37] WPIDS

AB US2005100965 A UPAB: 20050613

NOVELTY - A binding protein (I) capable of binding to human interleukin (IL)-18 protein, comprising an Ig constant heavy region, an Ig constant light region, an Ig variable heavy region, and an Ig variable light region, or an antigen binding domain capable of binding human interleukin (IL)-18, the antigen binding domain comprising at least one CDR chosen from CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2 and CDR-L3, is new.

DETAILED DESCRIPTION - A binding protein (I) capable of binding to human interleukin (IL)-18, comprising an Ig constant heavy region having a fully defined 330 amino acid (SEQ ID Number 2) or 330 amino acid (SEQ ID Number 3) given in the specification, an Ig constant light region having a fully defined 106 amino acid (SEQ ID Number 4) or 105 amino acid (SEQ ID Number 5) given in the specification, an Ig variable heavy region having a fully defined 121 amino acid (SEQ ID Number 6) given in the specification, and an Ig variable light region having fully defined 109 amino acid (SEQ ID Number 7) given in the specification, or an antigen binding domain capable of binding human IL-18, the antigen binding domain comprises at least one CDR comprising an amino acid sequence having a sequence of (SEQ ID Number 42-47).

X1-X2-X3-X4-X5-X6-X7 (SEQ ID Number 42).

X1 = Ser, Asn, His, Arg or Tyr;

X2 = Tyr, Gly, Arg, Ser or **Cys**;

X3 = Trp, Gly, Asp, Ser, Val or Ile;

X4 = Ile, His, Trp, Tyr, Met, Lys or Asp;

X5 = Gly, Tyr, Ser, Asn or His;

X6 = Trp or absent;and

X7 = Thr, Ser, Gly or absent.

X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-X17 (SEQ ID Number 43).

X1 = Phe, Tyr, His, Ser or Val;

X2 = Ile or Phe;
X3 = Tyr, Ser or Trp;
X4 = Pro, Tyr or Ser;
X5 = Gly, Ser, Arg or Asp;
X6 = Asp or Gly;
X7 = Ser, Thr, Gly or Arg;
X8 = Glu, Thr, Ile or Asn;
X9 = Thr, Tyr, Asn, Ile, Lys, or His;
X10 = Arg, Tyr or Ser;
X11 = Tyr, Asn or Ser;
X12 = Ser, Pro, Ala or Val;
X13 = Pro, Ser, or Asp;
X14 = Thr, Leu or Ser;
X15 = Phe, Lys or Val;
X16 = Gln, Ser or Lys; and
X17 = Gly or absent.
X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-X17-X18 (SEQ ID Number 44).
X1 = Val, Asp, Glu, Ser or Cys;
X2 = Gly, Arg, Asp, Ser, Lys, Leu Tyr, or Ala;
X3 = Ser, Gly, Gly, Tyr or Arg;
X4 = Gly, Ser, Tyr, Asn, Thr or Asp;
X5 = Trp, Ser, Ala, Gly, Tyr or Thr;
X6 = Tyr, Gly, Ser, Phe, Trp, or Asn;
X7 = Pro, Ser, Phe, Tyr, Val, Gly or Trp;
X8 = Tyr, Phe, Asp, Pro, Met, Ile or Asn;
X9 = Thr, Trp, Asp, Leu, Tyr, Glu, Pro, Phe, or Gly;
X10 = Phe, Asp, Tyr, His, Val, Tyr or absent;
X11 = Asp, Tyr, Phe, Leu, or absent;
X12 = Ile, Asp, Tyr or absent;
X13 = Tyr or absent;
X14 = Tyr or absent;
X15 = Gly or absent;
X16 = Met or absent;
X17 = Asp or absent; and
X18 = Val or absent.
X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-X17 (SEQ ID Number 45).
X1 = Arg or Lys;
X2 = Ala, Gly or Ser;
X3 = Ser;
X4 = Glu, Arg, Gln or His;
X5 = Ser, Ile, Thr or Asn;
X6 = Ile, Val, Leu or Phe;
X7 = Ser, Gly, Leu, Asn or Arg;
X8 = Ser, Gly, Tyr, Arg, Asn, His or Asp;
X9 = Asn, Gly, Tyr, Arg or Ser;
X10 = Leu, Tyr, Ser, or Asp;
X11 = Ala, Leu, Asn, Val, Gly or Asp;
X12 = Ala, Asn, Glu, Lys, Gly or absent;
X13 = Lys, Thr, Asn or absent;
X14 = Asn, Tyr, Thr, or absent;
X15 = Tyr, Leu or absent
X16 = Leu, Cys, Tyr or absent; and
X17 = Ala, Asp or absent.
X1-X2-X3-X4-X5-X6-X7 (SEQ ID Number 46).
X1 = Thr, Gly, Ser, Trp or Glu;
X2 = Ala, Val, Thr, Ile, or Leu;
X3 = Ser or Phe;

X4 = Thr, Ile, Asn, Ser, Arg or Tyr;
X5 = Arg or Leu;
X6 = Ala, Gln, Glu or Phe; and
X7 = Thr or Ser.
X1-X2-X3-X4-X5-X6-X7-X8-X9-X10 (SEQ ID Number 47).
X1 = Gln or Met;
X2 = Gln, His or Tyr;
X3 = Tyr, Asn, Gly, Ser or Arg;
X4 = Asn, His, Tyr, Asp, Gly, Val, Leu or Ile;
X5 = Asn, Gly, Ile, Tyr, Ser, Gln, Phe or Glu;
X6 = Trp, Ser, Thr, Leu, Ile, or Phe;
X7 = Pro, Leu, Thr, Asp or Ile;
X8 = Ser, Leu, Pro, Cys, Trp, Ile or Phe;
X9 = Ile, Thr, Ser or absent; and
X10 = Thr or absent.

INDEPENDENT CLAIMS are also included for the following:

(1) a neutralizing binding protein capable of neutralizing IL-18, comprising (I);

(2) a labeled binding protein comprising (I) conjugated to a detectable label;

(3) a conjugate binding protein comprising (I) conjugated to a therapeutic or cytotoxic agent;

(4) an isolated nucleic acid (N1) encoding (I);

(5) a vector (V1) comprising (N1);

(6) a host cell comprising (V1);

(7) producing (I);

(8) a binding protein produced using (H1);

(9) a crystallized binding protein (CP1) comprising (I) that exists as a crystal;

(10) a composition (C1)for the release of a binding protein, comprising a formulation comprising CP1, and an ingredient, and at least one polymeric carrier;

(11) regulating gene expression of a gene of interest; and

(12) a pharmaceutical composition comprising (I), and a carrier.

ACTIVITY - Antiarthritic; Antirheumatic; Antiallergic; Antiarteriosclerotic; Antiparkinsonian; Anabolic; Hypertensive; Anti-HIV; Cytostatic; Analgesic; Antibacterial; Immunosuppressive; Neuroprotective.

MECHANISM OF ACTION - Reduces IL-18 activity (claimed).

To test the ability of anti-IL18 antibodies to reduce lipopolysaccharide (LPS) induced lethality, mice were administered with anti-IL-18 antibodies or control antibodies in 500 micro l of 0.9 % saline. Then, the animals were injected with 20 mg/kg lipopolysaccharide. Four hours later blood was obtained and serum IFN gamma titer was determined by enzyme linked immunosorbent assay (ELISA). The results showed that mice treated with anti-IL-18 antibodies were protected from LPS-induced lethality.

USE - (I) is useful for reducing human IL-18 activity, which involves contacting human IL-18 with (I) such that human IL-18 activity is reduced. (I) is useful for reducing human IL-18 activity in a human subject suffering from a disorder in which IL-18 activity is detrimental, which involves administering (I) to the human subject such that human IL-18 activity in the human subject is reduced. (I) is useful for treating a subject for a disease or a disorder in which IL-18 activity is detrimental by administering (I) to the subject. The disorder is chosen from rheumatoid arthritis, allergic disease, atherosclerosis, Parkinson's disease, Addison's disease, AIDS, cancer, acute and chronic pain, sepsis, multiple sclerosis, etc. (I) is also useful for treating a patient suffering from a disorder in which IL-18

is detrimental, which involves administering (I) before, concurrent, or after the administration of a second agent chosen from antibody, or its fragment, capable of binding human IL-12, methotrexate, an antibody, or its fragment, capable of binding human TNF, corticosteroids, cyclosporin, rapamycin, FK506, and non-steroidal anti-inflammatory agents. (C1) is useful for treating a mammal. (All claimed.)
Dwg.0/0

L39 ANSWER 6 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-201775 [21] WPIDS
CROSS REFERENCE: 1999-024034 [02]; 1999-080758 [07]; 2004-201266 [19]
DOC. NO. NON-CPI: N2005-166077
DOC. NO. CPI: C2005-064337
TITLE: New single-chain antigen-binding polypeptide capable of site-specific conjugation to **polyalkylene** oxide polymer, useful for treating or preventing TNF-alpha related toxicity in mammal.
DERWENT CLASS: A25 A96 B04 D16 S03
INVENTOR(S): BASU, A; FILPULA, D R; WANG, M; YANG, K
PATENT ASSIGNEE(S): (BASU-I) BASU A; (FILP-I) FILPULA D R; (WANG-I) WANG M; (YANG-I) YANG K
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005042680	A1	20050224	(200521)*		73

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2005042680	A1	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
		CIP of	US 2001-791540	20010226
		CIP of	US 2001-791578	20010226
		CIP of	US 2003-423847	20030425
			US 2004-831063	20040423

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2005042680	A1	CIP of	US 6824782

PRIORITY APPLN. INFO: US 2004-831063 20040423; US
1997-44449P 19970430; US
1997-50472P 19970623; US
1997-63074P 19971027; US
1997-67341P 19971202; US
1998-69842 19980430; US
2001-791540 20010226; US
2001-791578 20010226; US
2003-423847 20030425
AN 2005-201775 [21] WPIDS

CR 1999-024034 [02]; 1999-080758 [07]; 2004-201266 [19]
AB US2005042680 A UPAB: 20050401
NOVELTY - Single-chain antigen-binding polypeptide (I) capable of site-specific conjugation to **polyalkylene** oxide polymer, having first and second polypeptides with antigen-binding portion of variable region of **antibody heavy** or **light chain**, and peptide linker linking first and second polypeptides, where (I) having at least one **Cys** residue capable of conjugating to **polyalkylene** oxide polymer, and having at least one antigen binding site, is new.

DETAILED DESCRIPTION - A single-chain antigen-binding polypeptide (I) capable of site-specific conjugation to a **polyalkylene** oxide polymer, comprises (a) a first polypeptide comprising an antigen-binding portion of a variable region of an **antibody heavy** or **light chain**, (b) a second polypeptide comprising an antigen-binding portion of a variable region of an **antibody heavy** or **light chain**, and (c) a peptide linker linking the first and second polypeptides, where (I) has at least one **Cys** residue which is capable of being conjugated to a **polyalkylene** oxide polymer, and has at least one antigen binding site, and where the **Cys** residue is located at position chosen from (i) a C-terminus of the **heavy chain** or **light chain** variable region, (ii) an N-terminus of the **heavy chain** or **light chain** variable region, (iii) any amino acid position of the peptide linker, (iv) both the N-terminus and C-terminus, (v) position 2 of the linker, (vi) both position 2 of the linker and the C-terminus, and their combinations, and where (I) binds to TNF- alpha .

INDEPENDENT CLAIMS are also included for the following:

(1) a conjugate (C1) comprising (I) and a **polyalkylene** oxide polymer, where the **polyalkylene** oxide polymer is covalently linked to (I);

(2) a polynucleotide (II) encoding (I);

(3) a replicable expression vector (III) comprising (II);

(4) producing (I);

(5) detecting (M1) TNF- alpha suspected of being in a sample, involves contacting the sample with a reagent comprising (I), and detecting whether (I) has bound to the TNF- alpha ;

(6) a protein (IV) comprising two or more (I), where each single-chain antigen-binding polypeptide is the same or different; and

(7) a polynucleotide encoding (IV).

ACTIVITY - Antibacterial; Immunosuppressive; Antimicrobial; Cytostatic; Gastrointestinal-Gen.; Respiratory-Gen. Endotoxemia was induced in C57/BL6 mice by injecting TNF- alpha into D-galactosamine (NGal) sensitized mice through the intraperitoneal route. C57/BL6 mice were injected intraperitoneally with different doses of native single-chain antigen-binding polypeptide (SCA), **PEG**-SCA, and Humira, 30 minutes prior to challenging the mice with a combination of recombinant human TNF- alpha (1 micro g/animal) and N-galactosamine (20 mg/animal). Surviving mice were euthanized after 24 hours. Injection of NGal and TNF together caused lethality in nearly all animals within 24 hours. The mice treated with both the E2E7 MAb and **PEG**-SCA compounds exhibited high survival rates at comparable doses.

MECHANISM OF ACTION - Inhibitor of TNF- alpha USE - (I) is useful for treating or preventing TNF- alpha related toxicity in a mammal, which involves administering (I) to the mammal at an amount effective to inhibit TNF- alpha activity in the mammal (claimed). (I) or (C1)

are useful for treating conditions such as sepsis, autoimmune diseases, infectious diseases, transplantation/rejection, malignancy, pulmonary and intestinal disorders.
Dwg.0/9

L39 ANSWER 7 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-573617 [59] WPIDS
DOC. NO. CPI: C2005-173597
TITLE: New polynucleotide encoding a mature modified epidermal growth factor, for producing a medicament for therapy and for diagnosing e.g. proliferative diseases, immune diseases, and vascular diseases.
DERWENT CLASS: A96 B04 B05 D16
INVENTOR(S): KONTERMAN, R; KONTERMANN, R
PATENT ASSIGNEE(S): (VECT-N) VECTRON THERAPEUTICS AG
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1557429	A1	20050727	(200559)*		50
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
WO 2005070960	A1	20050804	(200559)	EN	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1557429	A1	EP 2004-1454	20040123
WO 2005070960	A1	WO 2005-EP604	20050121

PRIORITY APPLN. INFO: EP 2004-1454 20040123
AN 2005-573617 [59] WPIDS
AB EP 1557429 A UPAB: 20050915
NOVELTY - A polynucleotide (I) chosen from polynucleotides encoding mature modified epidermal growth factor (EGF) having a fully defined 53 amino acid (SEQ ID No: 1-15) sequence, given in the specification, polynucleotides with coding sequences having a fully defined 159 base pair (SEQ ID No: 16-30) sequence, given in the specification, and encoding mature modified EGF, is new.

DETAILED DESCRIPTION - A new polynucleotide (I) is chosen from:

(i) polynucleotides encoding at least a mature modified epidermal growth factor (EGF) having a fully defined 53 amino acid (SEQ ID No: 1-15) sequence, given in the specification;

(ii) polynucleotides with a coding sequence having a fully defined 159 base pair (SEQ ID No: 16-30) sequence, given in the specification encoding at least the mature modified EGF;

(iii) a polynucleotide encoding a fragment or derivative of a mature modified EGF encoded by the polynucleotide, where the

derivative of one or more amino acid residues are conservatively substituted compared to the mature modified EGF with the proviso that the polypeptide positions 28 and 48 are not Lys, and the fragment or derivative has EGF receptor (EGFR) binding activity;

(iv) a polynucleotide encoding a modified EGF having EGFR binding activity, and that is 50 % identical to the polynucleotides; and

(v) a polynucleotide or its complementary strand having a complementary strand which hybridizes, preferably under stringent conditions to the polynucleotides encoding a modified EGF having EGFR binding activity.

INDEPENDENT CLAIMS are also included for the following:

(1) a vector (V1) containing (I);

(2) a host cell (H1) genetically engineered with (I) or (V1);

(3) producing a modified EGF encoded by (I), comprising culturing (H1) and recovering the modified EGF encoded by (I);

(4) producing (M1) cells capable of expressing modified EGF, comprising genetically engineering cells in vitro with (V1), where the modified EGF is encoded by (I);

(5) a modified EGF (II) having the amino acid sequence encoded by (I) or obtainable by (M1);

(6) a composition (C1) comprising one or more (II) or a fusion polypeptide and one or more further component chosen from liposomes, virosomes, microspheres, niosomes, dentrimers, stabilizers, buffers, excipients and additives;

(7) producing (M2) a modified binding polypeptide, which is suitable for site-directed coupling, comprising modifying a polynucleotide encoding the binding polypeptide, which is to be modified, by identifying within the reading frame of polynucleotide all codons with the sequence:

(8) (a) AAA and AAG encoding Lys and replacing this (these) codon(s) with (a) codon(s) NNN excluding AAA and AAG;

(9) (b) AAA and AAG encoding Lys and replacing this (these) codon(s) with (a) codon(s) NNN excluding AAA and AAG and all codons with the sequence CGT, CGC, CGA, CGG, AGA, and AGG encoding Arg and replacing this (these) codon(s) with (a) codon(s) NNN excluding CGT, CGC, CGA, CGG, AGA, and AGG;

(10) (c) GAT and GAG encoding Asp and replacing this (these) codon(s) with (a) codon(s) NNN excluding GAT and GAC and all codons with the sequence GAA and GAG encoding Glu and replacing this (these) codon(s) with (a) codon(s) NNN excluding GAA and GAG;

(11) (d) TGT and TGC encoding **Cys** and replacing all but one of this (these) codon(s) with (a) codon(s) NNN excluding TGT and TGC;

(12) (e) TCT, TCC, TCA, TCG, AGT and AGC encoding Ser and replacing all but one of this (these) codon(s) with (a) codon(s) NNN excluding TCT, TCC, TCA, TCG, AGT and AGC and all codons with the sequence ACT, ACC, ACA and ACG encoding Thr and replacing all but one of this (these) codon(s) with (a) codon(s) NNN excluding ACT, ACC, ACA and ACG;

(13) (f) ATG encoding Met and replacing all but one of this (these) codon(s) with (a) codon(s) NNN excluding ATG;

(14) (g) TAT and TAC encoding Tyr and replacing all but one of this (these) codon(s) with (a) codon(s) NNN excluding TAT and TAC;

(15) (h) TGG encoding Trp and replacing all but one of this (these) codon(s) with (a) codon(s) NNN excluding TGG, and/or (i) CAT and CAC encoding His and replacing all but one of this (these) codon(s) with (a) codon(s)NNN excluding CAT and CAC, where N is A, C, G or T; and

(16) use of a modified binding polypeptide or fusion polypeptide

(III) producable by (M3) for the manufacture of a medicament or diagnostic for the prevention, treatment or diagnosis of a disease, which is characterized by an increased or decreased amount of at least one binding partner of the binding polypeptide in diseased tissue or cells involved in the disease.

ACTIVITY - Cytostatic; Antimicrobial; Vasotropic; Antirheumatic; Antiarthritic; Antinflammatory. No supporting data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I), (II) Or its fusion polypeptide, or (C1) are useful for producing a medicament for the therapy of proliferative diseases, immune diseases, infectious diseases, vascular diseases, rheumatoid diseases, and diseases in which cells in or adjacent to the disease site show an increased expression of EGFR, or for the diagnosis of the diseases. The proliferative disease is chosen from lung cancer, liver cancer, head and neck cancer, bladder, cancer, prostate cancer, cervix cancer, endometrial cancer, colorectal adenoma and adenocarcinoma, gastric cancer, esophageal cancer, breast cancer, squamous carcinoma, glioblastomas and other high-grade primary brain tumors, chronic inflammatory proliferative diseases, vascular proliferative diseases and virus-induced proliferative diseases. (III) Is useful for manufacturing a medicament or diagnostic for the prevention, treatment or diagnosis of the diseases (claimed). (II) Is useful for site-specific coupling e.g., targeting ligands and modified human EGF and its fragments, suitable for site-specific coupling.

DESCRIPTION OF DRAWING(S) - The figure shows schematic representation of strategy to isolate side-chain deaminated ligands or side-chain decarboxylated ligands.

Dwg.1/6

L39 ANSWER 8 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-436935 [45] WPIDS

DOC. NO. CPI: C2005-134278

TITLE: Novel RGD comprising polypeptide having one or more binding peptides useful for diagnosing proliferative disease and in preparing medicament for therapy of proliferative diseases.

DERWENT CLASS: A96 B04 B05 D16

INVENTOR(S): HOELLIG, P; KONTERMANN, R

PATENT ASSIGNEE(S): (VECT-N) VECTRON THERAPEUTICS AG

COUNTRY COUNT: 109

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1538164	A1	20050608	(200545)*	EN	33
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
WO 2005054293	A1	20050616	(200545)	EN	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1538164	A1	EP 2003-27943	20031204
WO 2005054293	A1	WO 2004-EP13860	20041206

PRIORITY APPLN. INFO: EP 2003-27943 20031204
AN 2005-436935 [45] WPIDS
AB EP 1538164 A UPAB: 20050715
NOVELTY - A RGD comprising polypeptide (P1) having one or more binding peptides is new.

DETAILED DESCRIPTION - A RGD comprising polypeptide (P1) comprises one or more binding peptides having an amino acid sequence of formula (I) or formula (II):

X1-X2-X3-Y1-Y2-Y3-Y4-Y1-X4-X5-X6 (I)

X7-X8-X9-Y1-Y2-Y3-Y4-Y1-X10-Y1-X11 (II)

Y1 = **Cys**
Y2 = Arg
Y3 = Gly
Y4 = Asp
X1 = Ala, Leu, Phe or Ser, preferably Ala or Leu
X2 = Arg, Leu, Phe, Pro or Ser, preferably Arg or Ser
X3 = Ala, Gly, Leu, Ser, Tyr or Val, preferably Gly, Leu or Tyr
X4 = Gln, Phe, Ser or Val, preferably Phe or Val
X5 = Arg, Asp, Glu or Gln, preferably Asp or Gln
X6 = Ala, Gln, Glu, Gly, Phe or Val, preferably Ala, Gln or Gly
X7 = Glu, Phe, Pro or Val, preferably Glu or Val
X8 = Ala or **Cys**, preferably **Cys**
X9 = Asp, **Cys**, Gln or His, preferably Gln
X10 = Leu, Phe or Val, preferably Leu
X11 = Gln, Phe, Pro or Val, preferably Pro

Where X1-X11 and Y1-Y4 are independently of each other the D or L amino acid or the amino acid residue mimetic of the respectively indicated amino acid or the amino acid sequence which lacks 1 or 2, preferably one amino acid(s) from the N-terminus or C-terminus.

INDEPENDENT CLAIMS are also included for:
(1) a polynucleotide (I) encoding one or more of (P1);
(2) a vector (II) containing (I);
(3) a host cell (III) genetically engineered with (I) or (II);
(4) a transgenic non-human animal containing (I), (II) and/or (III);
(5) an **antibody** specifically binding to the amino acid sequence within (P1); and
(6) a composition (C1) comprising (P1) and at least one or more further components chosen from liposomes, virosomes, microspheres, niosomes, dentrimers, stabilizers, buffers, excipients and additives.

ACTIVITY - Cytostatic; Vasotropic; Antiinflammatory; Immunosuppressive; Antimicrobial; Antirheumatic; Osteopathic.

MECHANISM OF ACTION - None given.

USE - (P1) or (C1) is useful for the production of a medicament for the therapy of proliferative diseases, immune diseases, inflammatory diseases, where the immune disease is preferably immune diseases, infectious diseases, vascular diseases and rheumatoid disease, most preferably osteoarthritis and rheumatoid arthritis or diseases in which cells in or adjacent a disease site express alpha v beta 3 and/or alpha v beta 5 integrin. The proliferative disease is chosen from carcinomas of the gastrointestinal or colorectal tract, liver, pancreas, kidney, bladder, prostate, endometrium ovary, testes, melanoma, dysplastic oral mucosa, invasive oral cancers, small cell

and non-small cell lung carcinomas, hormone-dependent breast cancers, independent breast cancers, transitional and squamous cell cancers, neurological malignancies including neuroblastoma, gliomas, astrocytomas, osteosarcomas, soft tissue sarcomas, hemangiomas, endocrinological tumors, hematologic neoplasias including leukemias, lymphomas, and other myeloproliferative and lymphoproliferative diseases, carcinomas in situ, hyperplastic lesions, adenomas, fibromas, histiocytosis, chronic inflammatory proliferative diseases, vascular proliferative diseases and virus-induced proliferative diseases. (P1) or (C1) is useful for diagnosing proliferative diseases, immune diseases, infectious diseases, vascular diseases, rheumatoid diseases, inflammatory diseases and diseases associated with an increase or decrease of the expression of alpha v beta 3 and/or alpha v beta 5 integrin (all claimed).

ADVANTAGE - (I) exhibits high binding affinity with respect to alpha v beta 3 and/or alpha v beta 5 integrins, and can be easily produce in the stabilized form. (I) improves the therapeutic effect of the drug. In vivo analysis of the RGD comprising polypeptide in increasing antitumor effect of a drug was carried out in C26 colon carcinoma model as follows. Tumor cells were injected subcutaneously into nude mice. The tumor bearing mice were treated with free doxorubicin, doxorubicin loaded with liposomes lacking RGD10 lipoprotein liposomes, or doxorubicin-loaded RGD10-LP3 liposomes, where the doxorubicin loaded liposomes injected doxorubicin dose of 4 mg/kg body weight at day 1, 3 and 6 after tumor had reached a size of approximately 50-100 mm3. After 11 days, tumor growth was found to be inhibited by 45% in mice treated with doxorubicin loaded RGD10-LP3 liposome compared to mice treated with doxorubicin loaded liposomes lacking RGD10 liposomes. The improved antitumor effect was also reflected by a prolonged mean survival time, which was 18 days for animals treated with doxorubicin-loaded RGD10-LP3 liposomes, compared to 15 days for doxorubicin loaded liposomes lacking RGD10 liposomes. The results indicated that the doxorubicin-loaded RGD10-LP3 liposomes exhibited improved antitumor effect compared to free doxorubicin and liposomes lacking RGD10 lipopeptide.

DESCRIPTION OF DRAWING(S) - The figure is a graph representing antitumor effects of doxorubicin LP3-liopsomes (DOX-LP3 liposomes), DOX liposomes or free doxorubicin, in C26 murine colon carcinoma tumor model.

Dwg.8/8

L39 ANSWER 9 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-737199 [72] WPIDS
CROSS REFERENCE: 2004-142855 [14]; 2004-534127 [51]; 2005-306343 [31]
DOC. NO. CPI: C2004-259164
TITLE: Novel polymer-linked **antibody** single variable domain, in which polymer is linked to **cysteine** or lysine residue, useful for treating inflammation, cancer, autoimmune disorders, transplantation rejection, pulmonary disorder or hepatitis.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): BASRAN, A
PATENT ASSIGNEE(S): (DOMA-N) DOMANTIS LTD
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2004081026 A2 20040923 (200472)* EN 171
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004081026	A2	WO 2004-GB2829	20040630

PRIORITY APPLN. INFO: US 2004-535076P 20040108; WO 2003-GB2804 20030630; US 2003-509613P 20031008

AN 2004-737199 [72] WPIDS

CR 2004-142855 [14]; 2004-534127 [51]; 2005-306343 [31]

AB WO2004081026 A UPAB: 20050517

NOVELTY - A polymer-linked **antibody** single variable domain (I) having a half-life of 1.3 or more hours, where the polymer is linked to **antibody** single variable domain at a **cysteine** or lysine of the single **antibody** variable domain, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a **poly(ethylene** glycol) (**PEG**)-linked substance (PLS);

(2) a polypeptide (II) comprising an antigen binding site, where (II) comprises one or two **antibody** variable domains and (II) has a hydrodynamic size of 24 kDa or more and a half life of 1.3 or more hours, where each variable domain has an antigen binding site, and each variable domain binds antigen as a **antibody** single variable domain in the polypeptide;

(3) a polypeptide (III) comprising a binding site specific for TNF- alpha , the polypeptide comprising one or two **antibody** variable domains, where the polypeptide has a hydrodynamic size of 24 kDa or more and a half life of 1.3 or more hours;

(4) a homomultimer (IV) of **antibody** single variable domains, where the homomultimer has a hydrodynamic size of 24 kDa or more and a half life of 1.3 or more hours;

(5) a heteromultimer (V) of **antibody** single variable domains, having a hydrodynamic size of 24 kDa or more and a half life of 1.3 or more hours, where each variable domain has an antigen binding site, and each **antibody** single variable domain binds antigen as single **antibody** variable domain in the heteromultimer;

(6) an **antibody** single variable domain (VI) comprising one or more solvent-accessible lysine residue at a predetermined location in the **antibody** single variable domain which is linked to a **PEG** molecule;

(7) an **antibody** single variable domain multimer (VII), each member of the multimer comprising one or more solvent accessible lysine residue which is linked to a **PEG** molecule;

(8) an **antibody** single variable domain

homo-or-hetero-trimer or tetramer (VIII) comprising one or more solvent-accessible **cysteine** residue which is linked to a **PEG** molecule;

(9) a pharmaceutical formulation (F1) comprising a **PEG** -linked **antibody** single variable domain having a half life of 1.3 or more hours and a carrier, or comprising **PEG**-linked **antibody** single variable domain dimer having half life of 1.3 or more hours and having a hydrodynamic size of 24 kDa or more, and a carrier;

(10) a pharmaceutical formulation (F2) comprising a **PEG** -linked **antibody** single variable domain heterotrimer or homotrimer or heterotetramer or homotetramer, where each variable domain has an antigen binding site, and each variable domain binds antigen as a single variable domain;

(11) a pharmaceutical formulation (F3) comprising **PEG** -linked **antibody** single variable domain which is degraded by no more than 10% after administration of (F3) to the stomach of an animal or no more than 10% in vitro by exposure to a protease chosen from pepsin, trypsin, elastase, chymotrypsin, and carboxypeptidase, where if the protease is pepsin, then the **PEG**-linked **antibody** single variable domain is degraded by no more than 10% in the presence of pepsin at pH 2 for 30 minutes, and where if the protease is trypsin, elastase, chymotrypsin, and carboxypeptidase, then the **PEG**-linked **antibody** single variable domain is degraded by no more than 10% in the presence of trypsin, elastase, chymotrypsin, and carboxypeptidase at pH 8 for 30 minutes; and

(12) reducing (M1) the degradation of an **antibody** single variable monomer or multimer domain by a protease chosen from pepsin, trypsin, elastase, chymotrypsin, and carboxypeptidase comprising linking the single variable domain to one or more **PEG** polymer.

ACTIVITY - Antibacterial; Antiinflammatory; Immunosuppressive; Cytostatic; Antidiabetic; Antiarthritic; Antirheumatic; Respiratory-Gen.; Virucide; Hepatotropic. To test the efficacy of a PEGylated **antibody** single variable domain (dAb) in the therapeutic model of arthritis in the Tg197 model, heterozygous transgenic mice were divided into groups of 10 animals with equal numbers of male and females. Treatment was twice weekly with 4.6 mg/kg intraperitoneal injections of dAb. The arthritic scoring clearly demonstrated that PEGylated TAR1-5-19 inhibited the progression of arthritis in a therapeutic model.

MECHANISM OF ACTION - TNF modulator.

USE - (I) is useful for treating sepsis, inflammation, cancer, autoimmune disorders (e.g., diabetes or rheumatoid arthritis), transplantation rejection, pulmonary disorder or hepatitis, or for diagnosing above disorders.

ADVANTAGE - (I) exhibits specificity towards TNF alpha and increased stability towards the action of protease (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows VH or VL hetero or homodimeric **poly(ethylene** glycol)-linked **antibody** single variable domain. (Drawing includes non-English language text).

Dwg.7/16

L39 ANSWER 10 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-625832 [60] WPIDS
DOC. NO. CPI: C2004-225142
TITLE: Novel neutralizing **antibody** having

specificity for human IL-1 beta, comprising **heavy** or **light chain**, useful in treatment or prophylaxis of pathological disorder e.g., rheumatoid arthritis, Alzheimer's disease or cancer.

DERWENT CLASS: A96 B04 D16
INVENTOR(S): LAWSON, A D G; POPPLEWELL, A G
PATENT ASSIGNEE(S): (CLLT) CELLTECH R & D LTD
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004072116	A2	20040826	(200460)*	EN	74
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2004210776	A1	20040826	(200565)		
EP 1597282	A2	20051123	(200577)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004072116	A2	WO 2004-GB463	20040206
AU 2004210776	A1	AU 2004-210776	20040206
EP 1597282	A2	EP 2004-708808	20040206
		WO 2004-GB463	20040206

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2004210776	A1	Based on	WO 2004072116
EP 1597282	A2	Based on	WO 2004072116

PRIORITY APPLN. INFO: GB 2003-3337 20030213
AN 2004-625832 [60] WPIDS
AB WO2004072116 A UPAB: 20051014
NOVELTY - A neutralizing **antibody** (I) having specificity for human interleukin-1beta (IL-1 beta), comprising a **heavy** or **light chain**, where the variable domain of **heavy** or **light chain** has one or more of CDR sequence for CDR-H1-H3 or CDR-L1-L3, respectively, is new.
DETAILED DESCRIPTION - A neutralizing **antibody** (I) having specificity for human IL-1 beta , comprising a **heavy** or **light chain**, where the variable domain of the **heavy** or **light chain** comprises one or more of a CDR having a sequence of Gly-Phe-Asp-Phe-Ser-Arg-Tyr-Asp-Met-Ser (S1) or Arg-Thr-Ser-Gly-Asn-Ile-His-Asn-Tyr-Leu-Thr (S2) for CDR-H1 or CDR-L1, a CDR having a sequence of Tyr-Ile-Ser-Ser-Gly-Gly-Gly-Ser-Thr-Tyr-Phe-Pro-Asp-Thr-Val-Lys-Gly (S3) or Asn-Ala-Lys-Thr-Leu-Ala-Thr (S4) for CDR-H2 or CDR-L2 and a CDR having the sequence given in

Gln-Asn-Lys-Lys-Leu-Thr-Trp-Phe-Asp-Tyr (S5) or Gln-His-Phe-Trp-Ser-Leu-Pro-Phe-Thr (S6) for CDR-H3 or CDR-L3, respectively. Optionally, (I) is a modified Fab fragment having:

(a) a **heavy** and **light chain** comprising fully defined sequence of 119 (S7) and 108 (S8) amino acids as given in the specification, respectively and having at the C-terminal end of its **heavy chain** a modified hinge region containing one **cysteine** residue to which an effector or reporter molecule may be attached; or

(b) a **heavy** and **light chain** comprising fully defined sequence of 138 (S9) and 128 (S10) amino acids as given in the specification, respectively.

INDEPENDENT CLAIMS are also included for the following:

(1) a neutralizing **antibody** (II) having specificity to IL-1 beta , comprising a variable domain that is 90% or more identical or similar to (I) or that binds to the epitope which is similar to that of (I);

(2) an isolated DNA sequence (III) encoding the **heavy** and/or **light chain**(s) of (I) or (II);

(3) a cloning or expression vector (IV) comprising one or more of (III);

(4) a host cell (V) comprising one or more (IV);

(5) producing (I); and

(6) a pharmaceutical composition (VI) comprising (I) or (II) in combination with one or more of excipient, diluent or carrier.

ACTIVITY - Antiarthritic; Antirheumatic; Antiinflammatory; Neuroprotective; Nootropic; Immunosuppressive; Cytostatic.

MECHANISM OF ACTION - Immunotherapy. No supporting data is given.

USE - (I) or (V) is useful in treatment or prophylaxis of a pathological disorder that is mediated by IL-1 beta , or that is associated with an increased level of IL-1 beta (claimed). (I) is useful in treatment or prophylaxis of pathological disorder mediated by IL-1 beta e.g., arthritis, rheumatoid arthritis, pelvic inflammatory disease, Alzheimer's disease, Crohn's disease, pancreatitis, graft-versus-host disease or cancer. (I) is useful for diagnosing a diseased state in which IL-1 beta is involved or for producing medicament for treating or prophylaxis of pathological disorder.

DESCRIPTION OF DRAWING(S) - The figure shows the structure of a modified Fab fragment derived from an **antibody** IL-1 beta covalently linked by a **cysteine** residue to a lysyl-maleimide linker.

Dwg.12/12

L39 ANSWER 11 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-580636 [56] WPIDS

DOC. NO. CPI: C2004-211631

TITLE: Pharmaceutical composition for treating systemic lupus erythematosus (SLE), has salt of peptide corresponding to complementarity-determining region of **heavy/light chain** of anti-DNA 16/6 Id **antibody** that induces immune response to SLE.

DERWENT CLASS: A96 B04 D16

INVENTOR(S): COHEN-VERED, S; GILBERT, A; KLINGER, E; NAFTALI, E; WEINSTEIN, V

PATENT ASSIGNEE(S): (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM IND INC; (COHE-I) COHEN-VERED S; (GILB-I) GILBERT A; (KLIN-I) KLINGER E; (NAFT-I) NAFTALI E; (WEIN-I)

WEINSTEIN V; (TEVA-N) TEVA PHARM USA INC
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004064787	A2	20040805	(200456)*	EN	132
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW					
US 2005008634	A1	20050113	(200506)		
AU 2004206842	A1	20040805	(200562)		
EP 1594434	A2	20051116	(200575)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
NO 2005003773	A	20051012	(200577)		
BR 2004006745	A	20051220	(200604)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004064787	A2	WO 2004-US948	20040114
US 2005008634	A1 Provisional	US 2003-439918P	20030114
		US 2004-758397	20040114
AU 2004206842	A1	AU 2004-206842	20040114
EP 1594434	A2	EP 2004-702215	20040114
		WO 2004-US948	20040114
NO 2005003773	A	NO 2005-3773	20050808
BR 2004006745	A	BR 2004-6745	20040114
		WO 2004-US948	20040114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2004206842	A1 Based on	WO 2004064787
EP 1594434	A2 Based on	WO 2004064787
BR 2004006745	A Based on	WO 2004064787

PRIORITY APPLN. INFO: US 2003-439918P 20030114; US 2004-758397 20040114

AN 2004-580636 [56] WPIDS

AB WO2004064787 A UPAB: 20040901

NOVELTY - A pharmaceutical composition (I), comprising a salt of a peptide with 12-30 consecutive amino acids having a sequence corresponding to an amino acid sequence found within complementarity-determining region (CDR) of **heavy** or **light chain** of a human monoclonal anti-DNA 16/6 Id **antibody**, or a **heavy** or **light chain** of a pathogenic anti-DNA monoclonal **antibody** that induces systemic lupus erythematosus (SLE)-like disease response in mice.

DETAILED DESCRIPTION - A pharmaceutical composition (I), comprising an aqueous carrier, from 0.1-20 mg/ml of the composition of

a salt of:

(a) a peptide comprising at least 12 and at most 30 consecutive amino acids having a sequence corresponding to a sequence of the amino acids found within a complementarity-determining region (CDR) of a **heavy** or a **light chain** of a human monoclonal anti-DNA 16/6 Id **antibody**, or a **heavy** or **light chain** of a pathogenic anti-DNA monoclonal **antibody** that induces a systemic lupus erythematosus (SLE)-like disease response in mice; or

(b) a peptide comprising consecutive amino acids having the sequence:

(i) Thr-Gly-Tyr-Tyr-X1-X2-X3-X4-X5-Gln-Ser-Pro-Glu-Lys -Ser-Leu-Glu-Trp-Ile-Gly (S1);

(ii) Glu-Ile-Asn-Pro-Ser-Thr-Gly-Gly-X6-X7-X8-X9-X10-X11-X12-Lys -Ala-Lys-Ala-Thr (S2);

(iii) Tyr-Tyr-**Cys**-Ala-Arg-X13-X14-X15-X16-Pro-Tyr-Ala-X17-X18-Tyr-Trp-Gly-Gln-Gly-Ser (S3);

(iv) Gly-Tyr-Asn-X19-X20-X21-X22-X23-X24-Ser-His-Gly-X25-X26-Leu-Glu-Trp-Ile-Gly (S4);

(v) Tyr-Tyr-**Cys**-Ala-Arg-X27-X28-X29-Tyr-Gly-X30-X31-X32-Gly-Gln-Thr-Leu (S5);

(vi) X33-Tyr-Tyr-Trp-Ser-Trp-Ile-X34-Gln-X35;

(vii) Pro-X36-X37-Gly-X38-Glu-Trp-Ile-Gly (S6);

(viii) Tyr-Tyr-**Cys**-Ala-Arg-X39-Leu-Leu-X40-X41-X42-X43-X44-Asp-Val-Asp-Tyr-X45-Gly-46-Asp-Val (S7);

(ix) Phe-Ser-Gly-Tyr-Tyr-Trp-Ser (S8);

(x) Glu-Ile-Asn-His-Ser-Gly-Ser-Thr-Asn-Tyr-Lys-Thr-Ser-Leu-Lys-Ser (S9); or

(xi) Gly-Leu-Leu-Arg-Gly-Gly-Trp-Asn-Asp -Val-Asp-Tyr-Tyr-Tyr-Gly-Met-Asp-Val (S10); or

(c) a peptide comprising consecutive amino acids having the above sequences, or at least two of the sequences in (a), and (b) (i)-(x); or

(d) a peptide comprising consecutive amino acids having a sequence comprising at least two identical sequences included in (a) and (b) (i)-(x), and a solubility enhancer chosen from dimethyl-acetamide, **polyethylene** glycol, polyoxylated castor oil, N-methyl-2-pyrrolidinone, 1-ethenyl-2- pyrrolidinone, **polyoxyethylene** sorbitan esters and a substituted beta -cyclodextrin, where both the peptide and the solubility enhancer are dissolved in the aqueous carrier, and where the composition has a pH between 4 and 9.

X1 = Met, Ala or Val;
X2 = Gln, Asp, Glu or Arg;
X3 = Trp or Ala;
X4 = Val or Ser;
X5 = Lys, Glu or Ala;
X6 and X7 = Thr, Val or Ala;
X8 = Tyr or Phe;
X9 = Asn or Asp;
X10 = Gln or Glu;
X11 = Lys or Glu;
X12 = Phe or Tyr;
X13 = Phe, Thr or Gly;
X14 = Leu, Ala or Ser;
X15 = Trp or Ala;
X16 = Glu or Lys;
X17 = Met or Ala;
X18 = Asp, Lys or Ser;

X19 = Met or Ala;
X20 = Asn, Asp or Arg;
X21 = Trp or Ala;
X22 = Val or Ser;
X23 = Lys or Glu;
X24 = Gln or Ala;
X25 = Lys or Glu;
X26 = Ser or Ala;
X27 = Ser or Phe;
X28 = Gly or Ala;
X29 = Arg, Ala or Glu;
X30 = Asn or Asp;
X31 = Tyr or Phe;
X32 = Trp, His or Ala;
X33 = Gly or Thr;
X34 = Arg or Lys;
X35 = Pro or Ser;
X36 = Gly or Glu;
X37 = Lys or Asp;
X38 = Glu, Leu or Ser;
X39 = Gly or Phe;
X40 = Arg or Ala;
X41 = Gly or Ala;
X42 = Gly or Ala;
X43 = Trp or Ala;
X44 = Asn or Ala;
X45 = Tyr or Trp; and
X46 = Met or Gln;

INDEPENDENT CLAIMS are also included for:

(1) manufacturing (M1) (I), involves preparing a solution of dimethyl-acetamide, polyethylene glycol, polyoxylated castor oil, N-methyl-2-pyrrolidinone, 1-ethenyl-2-pyrrolidinone, polyoxyethylene sorbitan esters, or a substituted beta -cyclodextrin in an aqueous carrier at a predetermined concentration, adding a predetermined amount of a salt of (I) (a)-(I)(d), adjusting the pH of the solution containing (I) (b), until the peptide dissolves in the solution, and if necessary, adjusting the pH of the solution containing (I)(c) to a pH of 4-9, thus manufacturing the pharmaceutical composition;

(2) a composition (II) prepared by (M1);

(3) a lyophilized pharmaceutical composition comprising from 0.1-20 mg/ml of the (I);

(4) lyophilizing (M2) (I);

(5) a lyophilized pharmaceutical composition (III) prepared by (M2); and

(6) a packaged pharmaceutical composition, comprising a packaging material, and a predetermined amount of (III).

ACTIVITY - Antiinflammatory; Dermatological; Immunosuppressive.

MECHANISM OF ACTION - Inducer of immune response to SLE-inducing auto antibodies; Inhibitor of T cell proliferative responses.

The effect of hCDR peptides on the secretion of interleukin-2 (IL-2) by peripheral blood lymphocytes (PBL) in SLE patients was tested as follows. PBL of SLE patients were incubated with the human 16/61d mAb in the absence or presence of the peptides hCDR1 or hCDR3. Supernatants of the cultures were collected following 48 hours of incubation. Assays of determine levels of IL-2 in the supernatants were performed using the CTLL IL-2 dependent line. The cells of the CTLL line (2 multiply 104/well) were incubated in the presence of the different supernatants for 24 hours, followed by the addition of 3H-thymidine for an additional 18-hour incubation period. Cells were

then harvested and radioactivity counted used a beta -counter. Results were calculated based on recombinant human IL-2 used as a standard. The ability of the peptides to inhibit the IL-2 secretion of PBL of 23 responders stimulated by the human 16/6 Id was tested. The results showed that hCDR1 and hCDR3 inhibited the secretion of IL-2 by PBL of 21/23 and 19/23 patients, respectively. Thus, inhibition of proliferative responses of PBL directly was found to be correlated with IL-2 inhibition by the CDR-based peptides.

USE - (I) is useful for treating SLE and for alleviating symptoms of SLE in a human subject, which involves administering (I) to the human subject (claimed).

DESCRIPTION OF DRAWING(S) - The figure is a graph showing the proliferation of PBL in systemic lupus erythematosus (SLE) patient stimulated with mitogen phytohemagglutinin (PHA) in the absence or presence of hCDR1 or hCDR3.

Dwg.9/17

L39 ANSWER 12 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-553599 [53] WPIDS
DOC. NO. CPI: C2004-202592
TITLE: Treating or preventing a lung disease comprises administering to the subject a compound comprising a therapeutic agent and a targeting element directed to a ligand.
DERWENT CLASS: B04 D16
INVENTOR(S): HENDERSON, D R
PATENT ASSIGNEE(S): (ARIZ-N) ARIZEKE PHARM INC
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004062603	A2	20040729	(200453)*	EN	108
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2005036951	A1	20050217	(200514)		
AU 2004204764	A1	20040729	(200562)		
EP 1589943	A2	20051102	(200573)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2004062603	A2		WO 2004-US445	20040109
US 2005036951	A1	Provisional	US 2003-439373P	20030109
		Provisional	US 2003-480047P	20030620
		Provisional	US 2003-494841P	20030812
			US 2004-754485	20040109
AU 2004204764	A1		AU 2004-204764	20040109
EP 1589943	A2		EP 2004-701216	20040109
			WO 2004-US445	20040109

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2004204764	A1 Based on	WO 2004062603
EP 1589943	A2 Based on	WO 2004062603

PRIORITY APPLN. INFO: US 2003-494841P 20030812; US 2003-439373P 20030109; US 2003-480047P 20030620; US 2004-754485 20040109

AN 2004-553599 [53] WPIDS

AB WO2004062603 A UPAB: 20040818

NOVELTY - Treating or preventing a lung disease in a subject comprises administering to the subject via a pulmonary, oropharyngeal, or nasopharyngeal route a compound comprising a therapeutic agent and a targeting element directed to a ligand, where the targeting element confers apical to basolateral transcytosis to the therapeutic agent in an in vitro transcytotic assay.

ACTIVITY - Antimicrobial; Antitubercular; Tuberculostatic; Virucide; Fungicide; Antiinflammatory; Respiratory-Gen; Antiasthmatic.

No biological data given.

MECHANISM OF ACTION - None given.

USE - The method is useful for treating or preventing a lung disease in a subject. The method, compound or composition are useful for treating or preventing a lung disease, e.g. a respiratory tract infection, an infection of the lung, or a bacterial infection that causes tuberculosis, a viral infection that causes severe acute respiratory syndrome (SARS), fungal infection, causes pneumonia, a disorder of the interstitium, a disorder of gas exchange or blood circulation, a disease of the airways, a disorder of the pleura, Chronic Obstructive Pulmonary Disorder (COPD), or asthma.

Dwg.0/8

L39 ANSWER 13 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-364854 [34] WPIDS

DOC. NO. NON-CPI: N2004-291824

DOC. NO. CPI: C2004-137729

TITLE: Probe useful for detecting presence or absence of target ligand and target reaction inducing agent, comprises first pair of nucleic acid sequences, recognition element conjugated to first sequence and detectable label producing signal.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): CHUN, K H; HWANG, H J

PATENT ASSIGNEE(S): (AHRA-N) AHRAM BIOSYSTEMS INC

COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004033476	A1	20040422	(200434)*	EN	286

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003269522 A1 20040504 (200465)
US 2005118603 A1 20050602 (200537)
EP 1558626 A1 20050803 (200551) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004033476	A1	WO 2003-KR2101	20031011
AU 2003269522	A1	AU 2003-269522	20031011
US 2005118603	A1 Provisional	US 2002-417864P	20021011
	CIP of	US 2003-684230	20031010
		US 2003-684346	20031010
EP 1558626	A1	EP 2003-751517	20031011
		WO 2003-KR2101	20031011

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003269522	A1 Based on	WO 2004033476
EP 1558626	A1 Based on	WO 2004033476

PRIORITY APPLN. INFO: US 2002-417864P 20021011; US 2003-684230 20031010; US 2003-684346 20031010

AN 2004-364854 [34] WPIDS

AB WO2004033476 A UPAB: 20040527

NOVELTY - A probe comprises a first pair of nucleic acid sequences consisting of a first object and complement sequence complementary to each other and forming a first hybridized duplex, a recognition element conjugated to first sequence, a detectable label producing a characteristic signal, is new.

DETAILED DESCRIPTION - A probe (I) comprises at least one and preferably all of the following as operably linked components, a first pair of nucleic acid sequences consisting of a first object sequence and a first complement sequence, the first object and first complement sequences each independently having 3-150 nucleotides, being substantially complementary to each other, and forming a first hybridized duplex, a recognition element conjugated to at least one of the first object and first complement sequences, the recognition element specifically interacting with at least one target agent, an optionally detectable label producing a characteristic signal whose level is a function of the amount of the first hybridized duplex, where in the presence of the target agent, the interaction of the target agent with the recognition element alters the amount of the first hybridized duplex compared to that in the absence of the target agent, altering the characteristic signal.

INDEPENDENT CLAIMS are included for the following:

(1) a kit comprising (I) and instructions for performing an assay for detecting a target agent or target ligand, or for detecting inhibitors or enhancers that inhibit or enhance interaction of target agent with the recognition element; and

(2) a target detection system comprising (I).

(3) a method for detecting in a sample the presence or absence of at least one target receptor agent that can selectively bind to a probe ligand, a target reaction inducing agent that can specifically

cleave a cleavage site or induce a covalent coupling of a reaction site under the conditions including a detection temperature;

(4) a method for detecting in a sample the presence or absence of at least one target ligand under the conditions including a detection temperature;

(5) a method for detecting in a sample the presence or absence of a target reaction inducing agent that can specifically convert a reaction site to a conjugation or non-conjugatable site under the conditions including a detection temperature;

(6) a method for detecting an inhibitor or enhancer for binding of a receptor agent to a probe ligand, for a reaction inducing agent that can specifically cleaved a cleavage site under the conditions including a detection temperature; and

(7) a method for detecting an inhibitor or enhancer for reaction inducing agent that can specifically induce a covalent coupling of reaction site or convert a reaction site to a conjugation or a non-conjugatable site under the conditions including a detection temperature.

USE - (I) is useful for detecting in a sample the presence or absence of at least one target receptor agent that can selectively bind to a probe ligand, a target reaction inducing agent that can specifically cleave a cleavage site or induce a covalent coupling of a reaction site under the conditions including a detection temperature. (I) is useful for detecting in a sample the presence or absence of at least one target ligand under the conditions including a detection temperature. (I) is also useful for detecting in a sample the presence or absence of a target reaction inducing agent that can specifically convert a reaction site to a conjugation or non-conjugatable site under the conditions including a detection temperature.

(I) is useful for detecting an inhibitor or enhancer for binding of a receptor agent to a probe ligand, for a reaction inducing agent that can specifically cleaved a cleavage site under the conditions including a detection temperature. (I) is also useful for detecting an inhibitor or enhancer for reaction inducing agent that can specifically induce a covalent coupling of reaction site or convert a reaction site to a conjugation or a non-conjugatable site under the conditions including a detection temperature (all claimed).

(I) is useful for detecting a wide spectrum of target agents in a biological, pharmaceutical, industrial, or environmental sample.

DESCRIPTION OF DRAWING(S) - The figure shows a schematic representation of non-competitive version of an affinity probe for detecting binding of a receptor agents in the hybridized and dissociated conformations.

first complement sequence 2a
recognition element 3
coupling element 4
receptor agent 10
probe ligand 11
Dwg.1/52

L39 ANSWER 14 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-340193 [31] WPIDS
DOC. NO. CPI: C2004-129046
TITLE: Novel bispecific molecule comprising a first recognition binding moiety that binds C3b-like receptor, cross-linked through a **polyethylene** glycol linker to second recognition binding moieties that bind molecules other than C3b-like receptors.
DERWENT CLASS: A96 B04 B05 D16

INVENTOR(S): CASEY, L; LEE, L S; MOHAMED, N; PORTER, J P; SESAY, M; WANG, X
PATENT ASSIGNEE(S): (ELUS-N) ELUSYS THERAPEUTICS INC
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004024889	A2	20040325	(200431)*	EN	95
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003270686	A1	20040430	(200462)		
EP 1539811	A2	20050615	(200539)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
JP 2005539067	W	20051222	(200604)		64

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004024889	A2	WO 2003-US29059	20030916
AU 2003270686	A1	AU 2003-270686	20030916
EP 1539811	A2	EP 2003-752394	20030916
		WO 2003-US29059	20030916
JP 2005539067	W	WO 2003-US29059	20030916
		JP 2004-536556	20030916

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003270686	A1	Based on	WO 2004024889
EP 1539811	A2	Based on	WO 2004024889
JP 2005539067	W	Based on	WO 2004024889

PRIORITY APPLN. INFO: US 2002-411731P 20020916
AN 2004-340193 [31] WPIDS
AB WO2004024889 A UPAB: 20040514
NOVELTY - A bispecific molecule (I) comprising a first recognition binding moiety (B1) that binds a C3b-like receptor, and one or more second recognition binding moieties (B2) that bind a molecule, the molecule being other than a C3b-like receptor, where B1 is cross-linked through a **poly**-(**ethylene**) glycol (**PEG**) linker to B2, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing (M1) a population of (I) involves contacting an **antibody** that binds a C3b-like receptor with one or more recognition binding moieties, where the **antibody** is conjugated with a bifunctional **PEG** linker, and where the one more recognition binding moieties are derivatized to react with the bifunctional **PEG** linker, and where the one or more recognition binding moieties bind a molecule; under conditions such

that the derivatized recognition binding moieties react to form a covalent linkage with the **PEG** linker, thereby producing a population of bispecific molecules;

(2) a population of bispecific molecules produced by (M1);

(3) producing (M2) a population of **antibodies** that bind a C3b-like receptor comprising a **polyethylene** glycol linker, involves contacting the **antibodies** with a **polyethylene** glycol linker, such that the **antibodies** are derivatized at one or more sites with the **polyethylene** glycol liner, thereby producing a population of **PEG** -derivatized **antibodies**;

(4) population of the **PEG**-derivatized **antibodies** produced by (M2);

(5) a pharmaceutical composition comprising (I) and a carrier;

(6) a kit comprising a first container containing a **polyethylene** glycol-derivatized anti-CR1 **antibody**, a second container comprising a recognition binding moiety which is other than an anti-CR1 **antibody** and a third container comprising a derivatizing agent suitable to derivatize the one or more recognition binding moieties;

(7) a compound of formula called F1; and

(8) an **antibody** derivatized with F1.

R = phenyl, naphthyl or aromatic heterocycle each of which are substituted by at least one -C(O)H or -NHNH2.

ACTIVITY - Antibacterial; Virucide; Fungicide; Protozoacide; Antibacterial; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Pathogenic antigenic molecule binder.

USE - (I) is useful for treating disorder in a mammal, that is associated with the presence of the molecule in the circulation of the mammal (claimed).

(I) is preferably useful for treating or preventing disease or disorder associated with presence of pathogenic antigenic molecule, where the pathogenic antigenic molecule includes pathogenic antigenic molecule associated with parasite, fungus, protozoa, bacteria or virus; toxins, immune complexes, auto **antibodies**, drugs; non-pathogenic antigens such as transplantation antigens, where the bispecific molecules are useful for treating transplantation rejection. Preferably, the molecules are useful for treating anthrax infection.

Dwg.0/0

L39 ANSWER 15 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-239110 [22] WPIDS

DOC. NO. CPI: C2004-093604

TITLE: New adzyme for enzymatically altering a substrate, useful for preparing a composition for treating diseases associated with a soluble or membrane bound molecule, e.g. allergic or inflammatory diseases.

DERWENT CLASS: B04 D16

INVENTOR(S): AFEYAN, N B; BAYNES, B; DASGUPTA, R; LEE, F D; WONG, G G; DAS GUPTA, R; DAS, G R

PATENT ASSIGNEE(S): (AFEY-I) AFEYAN N B; (BAYN-I) BAYNES B; (DASG-I) DASGUPTA R; (LEEF-I) LEE F D; (WONG-I) WONG G G; (GUPT-I) DAS GUPTA R; (COMP-N) COMPOUND THERAPEUTICS INC

COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004019878	A2	20040311	(200422)*	EN	122
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004081647	A1	20040429	(200429)		
US 2004081648	A1	20040429	(200429)		
AU 2003262937	A1	20040319	(200462)		
US 2005074865	A1	20050407	(200525)		
EP 1539941	A2	20050615	(200539)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
JP 2005537032	W	20051208	(200580)		151

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2004019878	A2		WO 2003-US26937	20030827
US 2004081647	A1	Provisional	US 2002-406517P	20020827
		Provisional	US 2002-423754P	20021105
		Provisional	US 2002-430001P	20021127
			US 2003-650591	20030827
US 2004081648	A1	Provisional	US 2002-406517P	20020827
		Provisional	US 2002-423754P	20021105
		Provisional	US 2002-430001P	20021127
			US 2003-650592	20030827
AU 2003262937	A1		AU 2003-262937	20030827
US 2005074865	A1	Provisional	US 2002-406517P	20020827
		Provisional	US 2002-423754P	20021105
		Provisional	US 2002-430001P	20021127
		CIP of	US 2003-650592	20030827
			US 2004-792498	20040302
EP 1539941	A2		EP 2003-791885	20030827
			WO 2003-US26937	20030827
JP 2005537032	W		WO 2003-US26937	20030827
			JP 2004-569756	20030827

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003262937	A1	Based on	WO 2004019878
EP 1539941	A2	Based on	WO 2004019878
JP 2005537032	W	Based on	WO 2004019878

PRIORITY APPLN. INFO: US 2002-430001P 20021127; US 2002-406517P 20020827; US 2002-423754P 20021105; US 2003-650591 20030827; US 2003-650592 20030827; US 2004-792498 20040302

AN 2004-239110 [22] WPIDS

AB WO2004019878 A UPAB: 20040331

NOVELTY - An adzyme for enzymatically altering a substrate comprises a catalytic domain that catalyzes a chemical reaction converting the substrate to one or more products, and a targeting group that reversibly binds with an address site on the substrate or with an address site on a second molecule that occurs in functional proximity to the substrate (the targeting moiety and the catalytic domain are heterologous with respect to each other).

DETAILED DESCRIPTION - An adzyme for enzymatically altering a substrate comprises a catalytic domain that catalyzes a chemical reaction converting the substrate to one or more products, and a targeting moiety that reversibly binds with an address site on the substrate or with an address site on a second molecule that occurs in functional proximity to the substrate, where the targeting moiety and the catalytic domain are heterologous with respect to each other, the targeting moiety, when provided separately, binds to the substrate, the catalytic domain, when provided separately, catalyzes the chemical reaction converting the substrate to one or more products. The adzyme has one or more properties, with respect to the reaction with the substrate, of:

(a) a potency at least 2 times greater than the catalytic domain or the targeting moiety alone;

(b) a kon of 103 M-s-1 or greater;

(c) a kcat of 0.1 sec-1 or is greater;

(d) a KD that is at least 5 fold less than the Km of the catalytic domain;

(e) a k0ff of 10-4 sec-1 or greater;

(f) a catalytic efficiency at least 5 fold greater than the catalytic efficiency of the catalytic domain alone;

(g) a Km at least 5 fold less than the Km of the catalytic domain alone; and/or

(h) an effective substrate concentration that is at least 5 fold greater than the actual substrate concentration.

INDEPENDENT CLAIMS are also included for:

(1) an adzyme preparation for therapeutic use in a human patient comprising the adzyme;

(2) a method of making a medicament for use in treating a disorder that is associated with an activity of the substrate of the adzyme;

(3) a method of making a medicament for use in treating an inflammatory or allergic disorder;

(4) a method of treating a disorder that is associated with an activity of the substrate of the adzyme;

(5) a method of treating an inflammatory of allergic disorder;

(6) a nucleic acid comprising a coding sequence for the adzyme;

(7) an expression vector comprising the nucleic acid;

(8) a cell comprising the expression vector;

(9) a method for manufacturing an adzyme;

(10) a method of designing and constructing an effective adzyme; and

(11) a method of operating a therapeutic adzyme business.

ACTIVITY - Antiallergic; Antiinflammatory.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The adzyme is useful for preparing a composition for treating diseases associated with a soluble or membrane bound molecule, e.g., allergic or inflammatory disease.

Dwg.0/16

L39 ANSWER 16 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-226853 [21] WPIDS
DOC. NO. CPI: C2004-089498
TITLE: New purified or isolated IL-7 conformer comprising three disulfide bridges, useful for preventing or reducing opportunistic infections in immunodeficient patients, cancer patients, patients undergoing grafts.
DERWENT CLASS: B04 D16
INVENTOR(S): ASSOULINE, B; CORTEZ, P; GREGOIRE, A; MORRE, M C
PATENT ASSIGNEE(S): (CYTH-N) CYTHERIS; (ASSO-I) ASSOULINE B; (CORT-I) CORTEZ P; (GREG-I) GREGOIRE A; (MORR-I) MORRE M C
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004018681	A2	20040304	(200421)*	EN	110
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
EP 1391513	A1	20040225	(200421)	EN	53
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
AU 2003250216	A1	20040311	(200457)		
EP 1527179	A2	20050504	(200530)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
NO 2005000355	A	20050506	(200537)		
US 2005249701	A1	20051110	(200574)		
JP 2005534339	W	20051117	(200576)		66

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004018681	A2	WO 2003-EP8701	20030806
EP 1391513	A1	EP 2002-291996	20020808
AU 2003250216	A1	AU 2003-250216	20030806
EP 1527179	A2	EP 2003-792262	20030806
		WO 2003-EP8701	20030806
NO 2005000355	A	WO 2003-EP8701	20030806
		NO 2005-355	20050125
US 2005249701	A1 Provisional	US 2003-475881P	20030605
		WO 2003-EP8701	20030806
		US 2005-522883	20050418
JP 2005534339	W	WO 2003-EP8701	20030806
		JP 2004-530091	20030806

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003250216	A1 Based on	WO 2004018681
EP 1527179	A2 Based on	WO 2004018681
JP 2005534339	W Based on	WO 2004018681

Searcher : Shears 571-272-2528

PRIORITY APPLN. INFO: US 2003-475881P 20030605; EP 2002-291996 20020808
AN 2004-226853 [21] WPIDS
AB WO2004018681 A UPAB: 20040326
NOVELTY - A purified or isolated IL-7 conformer comprising three disulfide bridges, is new.
DETAILED DESCRIPTION - The purified or isolated IL-7 conformer comprise the following three disulfide bridges:
(a) **Cys**: 1-4 (Cys2- Cys92);
(b) 2-5 (Cys34-Cys129); and
(c) 3-6(Cys47-Cys141).
INDEPENDENT CLAIMS are included for the following:
(1) an IL-7 drug substance comprising, as the desired product, the IL-7 conformer, where the drug substance is substantially free of IL-7 molecular variants or product related impurities, and where the total amount of weight of IL-7 in the drug substance is at least 98, preferably 99.5 % by weight;
(2) a pharmaceutical composition comprising the drug substance and one or more carriers;
(3) a nucleic acid molecule encoding the IL-7 polypeptide, where the molecule comprises an altered Shine-Dalgarno-like sequence;
(4) a vector comprising the nucleic acid;
(5) a recombinant host cell comprising the nucleic acid or the vector;
(6) an **antibody** specifically immunoreactive with the IL-7 conformer;
(7) a method of producing an IL-7 drug substance or pharmaceutical composition; and
(8) a method of controlling an IL-7 containing preparation by determining the presence and/or relative quantity, in the preparation, of an IL-7 conformer.
ACTIVITY - Immunostimulant.
No biological data given.
MECHANISM OF ACTION - Immunostimulant.
USE - The conformer and pharmaceutical composition are useful for prophylactic or therapeutic stimulation of B or T lymphocyte development and proliferation, or for enhancement of global or specific immuno-reconstitution, or for enhancement of humoral or cellular immune response. They are also useful for preventing or reducing opportunistic infections in immunodeficient patients; for prolonging lymphopoiesis stimulation and/or producing specific immune response and/or to broaden the repertoire of a specific immune response in human patients, e.g. immunodeficient patients, cancer patients, patients undergoing grafts, patients infected with a virus or a parasite, elderly patients or any patients having low CD4 count (all claimed).
Dwg.0/18

L39 ANSWER 17 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-010089 [01] WPIDS
CROSS REFERENCE: 1999-045130 [04]; 2001-041267 [05]; 2001-122704 [13]; 2002-351262 [38]; 2003-767381 [72]
DOC. NO. NON-CPI: N2005-007942
DOC. NO. CPI: C2005-002825
TITLE: Composition useful in treating and/or diagnosing, for example, graft-versus-host disease or CD74-expressing malignancy, comprises immunoconjugate having anti-CD74 binding molecules conjugated to lipids,

polymeric carriers, and effectors.
DERWENT CLASS: A17 A23 A25 A96 B04 B07 D16 K08 T01
INVENTOR(S): GOLDENBERG, D M; GRIFFITHS, G L; HANSEN, H J; LUNDBERG, B B
PATENT ASSIGNEE(S): (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004219203	A1	20041104	(200501)*		44
WO 2004110390	A2	20041223	(200502)	EN	

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004219203	A1	Cont of	US 1999-307816	19990510
		Cont of	US 2000-590284	20000609
		Cont of	US 2001-965796	20011001
		Provisional	US 2002-360259P	20020301
		CIP of	US 2002-314330	20021209
		CIP of	US 2003-350096	20030124
		CIP of	US 2003-377122	20030303
		Provisional	US 2003-478830P	20030617
			US 2003-706852	20031112
WO 2004110390	A2		WO 2004-US19238	20040617

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2004219203	A1	Cont of	US 6306393

PRIORITY APPLN. INFO: US 2003-706852 20031112; US 1999-307816 19990510; US 2000-590284 20000609; US 2001-965796 20011001; US 2002-360259P 20020301; US 2002-314330 20021209; US 2003-350096 20030124; US 2003-377122 20030303; US 2003-478830P 20030617

AN 2005-010089 [01] WPIDS
CR 1999-045130 [04]; 2001-041267 [05]; 2001-122704 [13]; 2002-351262 [38]; 2003-767381 [72]
AB US2004219203 A UPAB: 20050112
NOVELTY - A composition (I) comprises an immunoconjugate which has one or more anti-CD74 binding molecules conjugated to one or more lipids, polymeric carriers, micelles, nanoparticles or their combinations, and one or more effectors.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing (M1) a carrier, involves mixing one or more amphiphilic lipids with an effector to form a carrier, and contacting the carrier with an anti-CD744 **antibody**; and

(2) a kit comprising (I).

ACTIVITY - Immunosuppressive; Cytostatic; Immunomodulatory.

In vitro analysis of the cytotoxic activity of free floxuridine (FUdR) and 3',5'-O-dioleoyl-FudR (FUdR-dO)-loaded emulsions and liposomes with and without coupled LL1 was performed on Raji human B-cell lymphoma lines, as follows. The cells (4 multiply 105) were plated in 24-well plates and incubated with drug containing preparations. Control experiments included free LL1 and drug free emulsions and liposomes. Cells were incubated for 24 hours at 37 deg. C in an atmosphere of 95% humidity and carbon dioxide (5%). The cells were washed twice before replacing with fresh media and incubated for an additional 48 hours. Then, tetrazolium dye was added, and formed reduction product was spun down, dissolved in EtOH:dimethyl sulfoxide (1:1) and read at 570 nm. The cytotoxic activity of FUdR-dO in LL1 conjugated emulsions and liposomes was tested and compared with the activity of unconjugated drug-carriers on Raji lymphoma cells. The result indicated an effective cytotoxic activity of FUdR-dO in both LL1-emulsions and LL1-liposomes, when compared with FUdR, where IC70 values were 0.45, 1.25, 5.3 and 7.3 micro M for FUdR-dO loaded LL1-emulsions, LL1-liposomes, emulsions and liposomes, respectively.

MECHANISM OF ACTION - Immunotoxin; Radioimmunotherapeutic.

USE - (I) is useful for treating and/or diagnosing a disease or disorder, which involves administering to a patient a therapeutic and/or diagnostic composition comprising (I), and an excipient. The disease or disorder is a CD74-expressing malignancy. The disease or disorder is chosen from an immune dysregulation disease, autoimmune disease, organ-graft rejection and graft-versus-host disease. The CD74-expressing malignancy is chosen from solid tumor, non- Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, B-cell malignancy, and T-cell malignancy. The disease or disorder is CD74-expressing malignancy other than lymphoma or leukemia. The CD74-expressing malignancy is a solid tumor, which is chosen from melanoma, carcinoma, sarcoma and glioma. The carcinoma is chosen from renal carcinoma, lung carcinoma, intestinal carcinoma, stomach carcinoma, breast carcinoma, prostate cancer, ovarian cancer, and melanoma. The CD74-expressing malignancy is a B-cell malignancy chosen from indolent forms of B-cell lymphomas, aggressive forms of B-cell lymphomas, chronic lymphatic leukemias, acute lymphatic leukemias and multiple myeloma. (I) comprises LL1 or its fragment. The composition further comprises one or more additional **antibodies** or their fragments chosen from anti-CD19, anti-CD20, anti-CD22, anti-CD30, anti-CD33, anti-CD52, anti-human leukocyte antigen (HLA)-DR, anti-MUC1, anti-TAC and their mixtures. The one or more of the additional **antibodies** are conjugated to one or more of the lipids, polymeric carriers, micelles, nanoparticles or their combinations. The effector molecule comprises one or more drugs, prodrugs, toxins, enzymes, radioisotopes, immunomodulators, cytokines, hormones, **antibodies**, oligonucleotides or their combinations (especially where the effector is FUdr, FUdr-dO or its mixtures).

The composition may further comprise one or more agents for photodynamic therapy, where the agent for photodynamic therapy is a photosensitizer, which comprises a benzoporphyrin monoacid ring A (BDP-MA), tin etiopurpurin (SnET2), sulfonated aluminum phthalocyanine (AISPc) and lutetium texaphyrin (Lutex). The composition comprises one

or more diagnostic agents. The composition comprises a diagnostic nuclide, which comprises 18F, 52Fe, 62Cu, 64Cu, 67Cu, 67Ga, 68Ga, 86Y, 89Zr, 94Tc, 94mTc, 99mTc, 111In, 123In, 123I, 124I, 125I, 131I or their mixtures. The diagnostic nuclide emits 25-4000 keV gamma particles and/or positrons. The diagnostic agent is used for performing positron emission tomography (PET). The method further involves performing PET. The diagnostic agent comprises one or more image enhancing agents and the method further involves performing magnetic resonance imaging (MRI). The image enhancing agent comprises gadolinium ions, lanthanum ions, manganese ions, iron, chromium, copper, cobalt, nickel, fluorine, dysprosium, rhenium, europium, terbium, holmium, neodymium or their mixtures. The composition comprises one or more radiopaque agents or contrast agents for X-ray or computed tomography (CT). The radiopaque or contrast agents include barium, diatrizoate, ethiodized oil, gallium citrate, iocarmic acid, iocetamic acid, iodamide, iodipamide, iodoxamic acid, iogulamide, iohexol, iopamidol, iopanoic acid, ioprocemic acid, iosefamic acid, ioseric acid, iosulamide meglumine, iosemetic acid, iotasul, iotetric acid, iothalamic acid, iotroxic acid, ioxaglic acid, ioxotrizoic acid, ipodate, meglumine, metrizamide, metrizoate, propyliodone, thallous chloride or their combinations. The composition comprises one or more ultrasound contrast agents, where the ultrasound contrast agent includes a liposome or dextran. The liposome is gas-filled.

The method further involves performing an operative, intravascular, laparoscopic or endoscopic procedure. The method further involves administering an additional composition, which comprises a therapeutic agent, diagnostic agent or their mixtures. The additional composition comprises an immunoconjugate, which comprises one or more anti-CD74 binding molecules conjugated to one or more lipids, polymeric carriers, micelles, nanoparticles or their combinations, and one more effectors. The anti-CD74 **antibody** or its fragment is conjugated to the therapeutic agent, diagnostic agent or their mixtures by chemical conjugation or genetic fusion. The additional composition comprises one or more drugs, prodrugs, toxins, enzymes, radioisotopes, immunomodulators, cytokines, hormones, **antibodies**, oligonucleotides or their combinations. The composition is administered before, during, simultaneously, or after the administration of the additional composition (all claimed).

ADVANTAGE - The immunoconjugate of (I) has a significant effect in evocation of a humoral and/or cellular immune response in a mammal.

DESCRIPTION OF DRAWING(S) - The figure shows a graph representing the dose-response curves for 3',5'-O-dioleoyl-floxuridine.

Dwg.9/9

L39 ANSWER 18 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER:	2004-201266 [19] WPIDS
CROSS REFERENCE:	1999-024034 [02]; 1999-080758 [07]; 2005-201775 [21]
DOC. NO. CPI:	C2004-079547
TITLE:	Novel single-chain antigen-binding polypeptide comprising first and second polypeptide comprising antigen-binding portion of variable region of **antibody heavy** or **light chain**, and peptide linker useful for treating sepsis.
DERWENT CLASS:	A96 B04 D16
INVENTOR(S):	BASU, A; FILPULA, D R; WANG, M; YANG, K
PATENT ASSIGNEE(S):	(BASU-I) BASU A; (FILP-I) FILPULA D R; (WANG-I) WANG M; (YANG-I) YANG K; (ENZO-N) ENZON PHARM INC
COUNTRY COUNT:	108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004009166	A1	20040115	(200419)*		48
WO 2004096989	A2	20041111	(200474)	EN	

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004009166	A1	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
		CIP of	US 2001-791578	20010226
			US 2003-423847	20030425
WO 2004096989	A2		WO 2004-US12458	20040423

PRIORITY APPLN. INFO: US 2003-423847 20030425; US 1997-44449P 19970430; US 1997-50472P 19970623; US 1997-63074P 19971027; US 1997-67341P 19971202; US 1998-69842 19980430; US 2001-791578 20010226

AN 2004-201266 [19] WPIDS

CR 1999-024034 [02]; 1999-080758 [07]; 2005-201775 [21]

AB US2004009166 A UPAB: 20050401

NOVELTY - A single-chain antigen-binding polypeptide (I) capable of site-specific conjugation to **polyalkylene** oxide polymer, comprising first polypeptide comprising antigen-binding portion of variable region of **antibody heavy/light chain**, second polypeptide comprising antigen-binding portion of variable region of **antibody heavy/light chain** and peptide linker linking first and second polypeptides, is new.

DETAILED DESCRIPTION - A single-chain antigen-binding polypeptide (I) capable of site-specific conjugation to a **polyalkylene** oxide polymer, comprising a first polypeptide comprising an antigen-binding portion of a variable region of an **antibody heavy** or **light chain**, a second polypeptide comprising an antigen-binding portion of a variable region of an **antibody heavy** or **light chain** and a peptide linker linking the first and second polypeptides, where the single-chain antigen-binding polypeptide has one or more **Cys** residue, which is capable of being conjugated to a **polyalkylene** oxide polymer, and has one or more antigen binding site and where the **Cys** residue is located at a

position chosen from a C-terminus of the **heavy chain** or **light chain** variable region, an N-terminus of the **heavy chain** or **light chain** variable region, any amino acid position of the peptide linker, both the N-terminus and C-terminus, position 2 of the linker, both position 2 of the linker of the C-terminus, and its combinations, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) a conjugate (II) comprising the (I) and **polyalkylene** oxide polymer, where the **polyalkylene** oxide polymer is covalently linked to the single-chain antigen-binding polypeptide at a **Cys** residue;

(2) polynucleotide (III) encoding (I);

(3) a replicable expression vector (IV) comprising (III);

(4) producing (M1) (I);

(5) protecting (M2) an antigen suspected of being in a sample, involves contacting a sample with a reagent comprising (I) or (II), where (II) is conjugated to **polyalkylene** oxide polymer, detecting whether (I) or (II) as bound to the antigen;

(6) a coating (V) comprising two or more (I) capable of site-specific conjugation to one or more **polyalkylene** oxide polymer; and

(7) a polynucleotide encoding (V).

ACTIVITY - Antiinflammatory; Immunosuppressive; Immunomodulator; Antibacterial; Antiulcer; Neuroprotective; Antirheumatic; Antiarthritic; Cytostatic; Anticoagulant.

MECHANISM OF ACTION - Protein therapy; Neutralization of TNF-alpha cellular cytotoxicity.

WEH-13VAR cells were seeded in a 96-well plate, 10000 cells per well and incubated overnight at 37 deg. C in a humidified incubator with 5% CO2. A range of concentrations of D2E7 single-chain antigen-binding (SCA) proteins and their PEGylated forms were added to the seeded cells in the 96-well plates in serial dilutions from 10 g/ml-2.5 ng/ml diluted in culture medium. Immediately following the addition of D2E7 SCA compounds, rhTNF- alpha was added to each well at a concentration of 1.0 ng/ml. The cells were then allowed to grow for 24 hour and cell viability was determined by addition of 15 mu l MTT dye reagent. The analysis of cell rescue was performed by comparing the viability of D2E7-treated cells with untreated cells in the presence of TNF- alpha . Control wells consisted of untreated cells, and cells treated with TNF- alpha alone. The cells in the control wells exhibited a complete loss of viability. The result showed that the D2E7 SCA compound effectively neutralized the cytokine and prevent its binding to the TNF- alpha receptors on these cells.

USE - (I) is useful for treating or diagnosing a disease or disorder in a mammal, which involves administering an effective amount of (I), where (I) binds to an antigen that is related to treating or diagnosing the disease or disorder (claimed).

(I) is useful for treating disease associated with sepsis include myocardial suppression, vascular leakage syndrome, organ necrosis, stimulation or the release of toxic secondary mediators and activation of the clotting cascade, endotoxic shock, gram negative sepsis and toxic shock syndrome, autoimmune disease, which include, tissue inflammation and joint destruction in rheumatoid arthritis, diabetes and multiple sclerosis, or disease associated with infectious disease which include TNF alpha -mediated brain inflammation, capillary thrombosis and infarction in malaria, meningitis, or disease associated with transplantation, rejection of transplants or side effects of the required immunosuppression agents which include TNF alpha -mediated allograft rejection and graft versus host disease

(GVHD), or malignancy such as TNF alpha -mediated cachexia, tumor growth, metastatic potential and cytotoxicity in malignancies, or pulmonary disorders such as adult respiratory distress syndrome or chronic pulmonary inflammatory disease, or intestinal disorders such as Crohn's disease and ulcerative colitis.

DESCRIPTION OF DRAWING(S) - The figure shows the scanned image intensity of the bands of D2E 2-7-SC-2 and PEGylated forms confirming reactivity of this anti-D2E7 antiserum with the recombinant SCA proteins and **PEG**-SCA conjugates.

Dwg.8/9

L39 ANSWER 19 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-071030 [07] WPIDS
CROSS REFERENCE: 2003-865093 [80]
DOC. NO. CPI: C2004-029346
TITLE: New recombinant protein **polyethylene** glycol positional isomer, useful for treating multi-organ failure, a disease mediated by TNF alpha, rheumatoid arthritis, osteoarthritis, or graft rejection,.
DERWENT CLASS: A25 A96 B04 D16
INVENTOR(S): MOZIER, N M
PATENT ASSIGNEE(S): (PHAA) PHARMACIA CORP; (CLLT) CELLTECH R & D LTD
COUNTRY COUNT: 104
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003099226	A2	20031204	(200407)*	EN	31
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003240790	A1	20031212	(200443)		
EP 1534753	A2	20050601	(200536)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
JP 2005529154	W	20050929	(200568)		22

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003099226	A2	WO 2003-US16619	20030528
AU 2003240790	A1	AU 2003-240790	20030528
EP 1534753	A2	EP 2003-731385	20030528
		WO 2003-US16619	20030528
JP 2005529154	W	WO 2003-US16619	20030528
		JP 2004-506753	20030528

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003240790	A1	Based on	WO 2003099226
EP 1534753	A2	Based on	WO 2003099226
JP 2005529154	W	Based on	WO 2003099226

Searcher : Shears 571-272-2528

PRIORITY APPLN. INFO: WO 2003-US8608 20030320; US 2002-383765P 20020528
AN 2004-071030 [07] WPIDS
CR 2003-865093 [80]
AB WO2003099226 A UPAB: 20051024
NOVELTY - A recombinant protein **polyethylene** glycol (**PEG**) positional isomer, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a therapeutic or diagnostic composition comprising a recombinant protein and at least one **PEG** positional isomer of the protein in combination with a pharmaceutical excipient, diluent, or carrier.
ACTIVITY - Immunosuppressive; Vasotropic; Antirheumatic; Antiarthritic; Osteopathic. No biological data given.
MECHANISM OF ACTION - TNF-inhibitor-alpha.
USE - The **antibody** is useful for treating multi-organ failure or a disease mediated by tumor necrosis factor (TNF) alpha , for reducing side effects associated with TNF alpha generation during neoplastic therapy, for eliminating or reducing shock-related symptoms associated with the treatment of prevention of graft rejection using an anti-lymphocyte **antibody**, or for diagnosing and imaging of disease states involving elevated TNF alpha levels. The **antibody** molecule is preferably used for treating rheumatoid arthritis or osteoarthritis.
Dwg.0/2

L39 ANSWER 20 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-865093 [80] WPIDS
CROSS REFERENCE: 2004-071030 [07]
DOC. NO. CPI: C2003-244476
TITLE: Novel recombinant protein disulfide isomer, useful for treating congestive heart failure, endotoxic shock, Crohn's disease, and autoimmune diseases, such as thyroiditis and rheumatoid and osteo-arthritis.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): BILD, G S; DUFIELD, R L; MO, J; MOZIER, N M
PATENT ASSIGNEE(S): (PHAA) PHARMACIA CORP; (CLLT) CELLTECH R & D LTD
COUNTRY COUNT: 104
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003080674	A1	20031002	(200380)*	EN	40
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003225900	A1	20031008	(200432)		
EP 1495056	A1	20050112	(200504)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2003080674	A1	WO 2003-US8608	20030320
AU 2003225900	A1	AU 2003-225900	20030320
EP 1495056	A1	EP 2003-745158	20030320
		WO 2003-US8608	20030320

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003225900	A1 Based on	WO 2003080674
EP 1495056	A1 Based on	WO 2003080674

PRIORITY APPLN. INFO: US 2002-366350P 20020320

AN 2003-865093 [80] WPIDS

CR 2004-071030 [07]

AB WO2003080674 A UPAB: 20050117

NOVELTY - A recombinant protein disulfide isomer, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a therapeutic or diagnostic composition (I) comprising a recombinant protein and a disulfide isomer of the protein in combination with an excipient, diluent or carrier;

(2) analyzing (M1) the characterization and quantitation of **antibody** fragment disulfide isomers comprises:

(a) pre-treating the **antibody** fragment with an organic solvent;

(b) digesting the pre-treated **antibody** fragment with proteases in the presence of the organic solvent; and

(c) a unit resolving the protease digest fragments; and

(3) analyzing (M2) the characterization and quantitation of **antibody** fragment degradation products and **antibody** fragment impurities in recombinant proteins chosen from methionyl oxidations, truncations, deamidation of asparagines, misincorporations, extensions or others involves pre-treating the protein with an organic solvent, digesting the pre-treated protein with proteases in the presence of the organic solvent and a unit resolving the protease digest fragments.

ACTIVITY - Antibacterial; Immunosuppressive; Cardiovascular-Gen.; Immunomodulator; Respiratory-Gen.; Antiinflammatory; Anti-HIV; Antipsoriatic; Antitubercular; Tuberculostatic; Anticoagulant; Hemostatic; Vulnerary; Antithyroid; Antirheumatic; Antiarthritic; Osteopathic.

MECHANISM OF ACTION - TNF alpha reducer. No supporting data is given.

USE - The recombinant protein is useful as a therapeutic and diagnostic agent (claimed). The recombinant protein which is an **antibody** is useful in the treatment of sepsis, congestive heart failure, septic or endotoxic shock, cachexia, adult respiratory distress syndrome, AIDS, allergies, psoriasis, tuberculosis (TB), inflammatory bone disorders, blood coagulation disorders, burns, rejection episodes following organ or tissue transplant, Crohn's disease and autoimmune diseases, such as thyroiditis and rheumatoid and osteo-arthritis. The **antibody** is also useful to reduce side effects associated with TNF alpha generation during neoplastic therapy, to eliminate or reduce shock-related symptoms associated with the treatment or prevention of graft rejection by use of an anti-lymphocyte **antibody**, or for treating multi-organ failure.

Dwg.0/5

L39 ANSWER 21 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-441133 [41] WPIDS
DOC. NO. CPI: C2003-116639
TITLE: Novel **antibody** molecules having specificity for human kinase insert domain-containing receptors, useful for treating inflammation, psoriasis, rheumatoid arthritis, tumor growth and metastasis.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): MORRISON, R K; POPPLEWELL, A G; TICKLE, S P; ZINKEWICH-PEOTTI, K
PATENT ASSIGNEE(S): (CLLT) CELLTECH R & D LTD; (MORR-I) MORRISON R K; (POPP-I) POPPLEWELL A G; (TICK-I) TICKLE S P; (ZINK-I) ZINKEWICH-PEOTTI K
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003031475	A2	20030417	(200341)*	EN	57
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
EP 1438340	A2	20040721	(200447)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
AU 2002334135	A1	20030422	(200460)		
BR 2002012756	A	20041116	(200501)		
HU 2004001618	A2	20041129	(200503)		
NO 2004000987	A	20040510	(200511)		
KR 2004097983	A	20041118	(200523)		
JP 2005516590	W	20050609	(200538)		33
ZA 2004001910	A	20050525	(200540)		68
MX 2004003274	A1	20040701	(200545)		
US 2005181448	A1	20050818	(200555)		
CN 1568331	A	20050119	(200572)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003031475	A2	WO 2002-GB4619	20021010
EP 1438340	A2	EP 2002-800666	20021010
		WO 2002-GB4619	20021010
AU 2002334135	A1	AU 2002-334135	20021010
BR 2002012756	A	BR 2002-12756	20021010
		WO 2002-GB4619	20021010
HU 2004001618	A2	WO 2002-GB4619	20021010
		HU 2004-1618	20021010
NO 2004000987	A	WO 2002-GB4619	20021010
		NO 2004-987	20040308
KR 2004097983	A	KR 2004-705051	20040406
JP 2005516590	W	WO 2002-GB4619	20021010
		JP 2003-534457	20021010

ZA 2004001910	A	ZA 2004-1910	20040309
MX 2004003274	A1	WO 2002-GB4619	20021010
		MX 2004-3274	20040406
US 2005181448	A1	WO 2002-GB4619	20021010
		US 2005-492228	20050215
CN 1568331	A	CN 2002-820210	20021010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1438340	A2 Based on	WO 2003031475
AU 2002334135	A1 Based on	WO 2003031475
BR 2002012756	A Based on	WO 2003031475
HU 2004001618	A2 Based on	WO 2003031475
JP 2005516590	W Based on	WO 2003031475
MX 2004003274	A1 Based on	WO 2003031475

PRIORITY APPLN. INFO: GB 2001-24317 20011010

AN 2003-441133 [41] WPIDS

AB WO2003031475 A UPAB: 20050112

NOVELTY - An **antibody** molecule having specificity for human kinase insert domain-containing receptor (KDR), comprising a **heavy chain** comprising a sequence of 444 or 235 amino acids fully defined in the specification, is new.

DETAILED DESCRIPTION - An **antibody** molecule having specificity for human kinase insert domain-containing receptor (KDR) (I) comprising:

(a) a **heavy chain** whose variable domain comprises a complementarity determining region (CDR) comprising a sequence CDRH1, CDRH2 or CDRH3;

(b) a **light chain** whose variable domain comprises a CDR comprising a sequence CDRL1, CDRL2 or CDRL3; or

(c) a **light chain** comprising a sequence of 235 or 249 amino acids fully defined in the specification and/or a **heavy chain** comprising a sequence of 444 amino acids fully defined in the specification.

Ser-Tyr-Gly-Met-Ser (CDRH1)

Thr-Ile-Thr-Ser-Gly-Gly-Ser-Tyr-Thr-Tyr-Tyr-Pro-Asp-Thr-Val-Lys-Gly (CDRH2)

Ile-Gly-Glu-Asp-Leu-Asp-Tyr (CDRH3)

Arg-Ala-Ser-Gln-Asp-Ile-Ala-Gly- Ser-Leu-Asn (CDRL1)

Ala-Thr-Ser-Ser-Leu-Asp-Ser (CDRL2)

Leu-Gln- Tyr-Gly-Ser-Phe-Pro-Pro-Thr (CDRL3)

INDEPENDENT CLAIMS are also included for:

(1) a variant (II) of (I), having an improved affinity for KDR;

(2) a compound (III) comprising (I) having covalently attached to an amino acid at or towards the C-terminal end of this **heavy chain**, an effector or reporter molecule;

(3) a DNA sequence (IV) encoding the **heavy** and/or **light chain** of (I);

(4) a cloning or expression vector (V) containing (IV);

(5) a host cell (VI) transformed with (V);

(6) producing (I); and

(7) a therapeutic or diagnostic composition comprising (I) or (III).

ACTIVITY - Antiinflammatory; Antipsoriatic; Antirheumatic; Antiarthritic; Cytostatic; Antitumor.

MECHANISM OF ACTION - Blocks vascular endothelial growth factor

(VEGF) binding to KDR; Vaccine.

The ability of VR165 **antibody** fragments to block VEGF binding to KDR was measured in a radioimmunoassay. VR165 **antibody** was conjugated to a branched molecule, **mPEG** (**polyethylene** glycol molecule)-lysyl bis-maleimide, and the conjugate was designated as DFM. Polyclonal anti Fc was used to capture seven Immunoglobulin (Ig)-domain KDR fused to human Fc in a microtiter plate, the **antibody** or its fragment was added, followed by the addition of 125-I labeled VEGF-165. Results of the assay were shown graphically. There was a superior blocking performance by DFM.

USE - (I) or (III) is useful for treating a pathology in which vascular endothelial growth factor (VEGF) and/or KDR are implicated, and in the manufacture of a medicament for the treatment of a pathology in which VEGF and/or KDR are implicated, which includes inflammation, psoriasis, rheumatoid arthritis, and tumor growth or metastasis (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the radioimmunoassay results, in which the **antibody** fragments are tested for blocking of vascular endothelial growth factor (VEGF) binding to KDR. Dwg.20/21

L39 ANSWER 22 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-554858 [52] WPIDS
DOC. NO. NON-CPI: N2003-440609
DOC. NO. CPI: C2003-149824
TITLE: Novel nucleic acid molecule encoding anti-platelet binding protein which is useful for inhibiting platelet aggregation or platelet mediated thrombus formation in blood and for treating venous thromboembolism.
DERWENT CLASS: A96 B04 D16 S03
INVENTOR(S): FILPULA, D R
PATENT ASSIGNEE(S): (FILP-I) FILPULA D R
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003027207	A1	20030206	(200352)*		30

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003027207	A1 Provisional	US 2000-185628P	20000229
		US 2001-794189	20010227

PRIORITY APPLN. INFO: US 2000-185628P 20000229; US 2001-794189 20010227
AN 2003-554858 [52] WPIDS
AB US2003027207 A UPAB: 20030813
NOVELTY - A nucleic acid molecule (I), or its complement, that encodes an anti-platelet binding protein, where (I) is isolated from a phage display library by an in vitro selection process that comprises screening a diverse human **antibody** variable domain expression library against at least one human platelet antigen, and the human **antibody** variable domain expression library

expresses single-chain proteins, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an expression vector (II) comprising (I) (or its complement) operably lined to a promoter;

(2) a host cell (III) comprising (II);

(3) a non-human mammal (IV) comprising cells transformed by (II) that produces the anti-platelet binding protein expressed by (II);

(4) a non-human transgenic mammal that comprises (II) that produces the anti-platelet binding protein expressed by (II);

(5) an anti-platelet binding protein (V) encoded by (I) that binds to activated or non-activated human platelet glycoprotein IIb/IIa receptor and inhibits platelet aggregation or thrombus formation;

(6) a composition comprising (V) and a carrier;

(7) a substantially isolated and purified human **antibody** (Ab) that binds to a platelet antigen that comprises an active antigen-binding site of (V);

(8) a human anti-platelet binding protein that comprises a fragment of Ab such as Fab fragment, Fv fragment, **light chain** fragment, **heavy chain** fragment, or their combination;

(9) a conjugate (VI) comprising a non-antigenic polymer covalently linked to the single-chain antigen-binding polypeptide (i.e. (V)); and

(10) producing an anti-platelet binding protein.

ACTIVITY - Thrombolytic; Antianginal; Cardiant; Cerebroprotective; Anticoagulant.

No biological data is given.

MECHANISM OF ACTION - Inhibitor of platelet aggregation or platelet mediated thrombus formation (claimed).

USE - (III) and (V) are useful for inhibiting platelet aggregation or platelet mediated thrombus formation in blood, by contacting the blood with an effective amount of (V) or host cells that produce (V). The blood is present in a mammal. The host cells are autologous to the mammal. The anti-platelet binding protein is present in the blood in a concentration of 1 pg-1 mg/ml of whole blood. (II) is useful for inhibiting platelet aggregation or platelet mediated formation of fibrin in a blood vessel, the blood vessel having an endothelial lining in need of treatment, by contacting the endothelial linking of the blood vessel with (II). The blood vessel is an autologous graft that is contacted with (II) before or after being grafted into a mammal in need of it. The mammal is a human. (All claimed.) (II), (III), (V) or (VI) is useful for preventing or treating conditions such as venous thromboembolism, unstable angina, saphenous vein bypass grafts, percutaneous transluminal coronary angioplasty, atrial fibrillation, valvular heart disease, cerebrovascular disease, peripheral vascular disease, secondary prevention of arterial thromboembolism, primary prevention of arterial thromboembolism, acute disseminated intravascular coagulation, chronic disseminated intravascular coagulation (Trousseau's syndrome). (III) and (V) are useful for coating surfaces of medical devices and/or appliances to prevent thrombus formation, prevent occlusion of extracorporeal devices, e.g. intravascular cannulas, prosthetic heart valves, vascular access shunts in hemodialysis patients, hemodialysis machines, and cardiopulmonary bypass machines, and for reducing the incidence of axillary-subclavian venous thrombosis in patients with long-term indwelling central vein catheters. (V) and (VI) are useful for treating anti-platelet binding protein-susceptible conditions or

conditions which would respond positively or favorably to anti-platelet binding protein based therapy. (V) is useful in diagnostic imaging and assays, both in vivo and in vitro, purification and isolation of platelet antigens, and as receptors in electronic biosensors, to purify and isolate platelet and related antigens, and in combination with, either conjugated or non-conjugated, other therapeutic or diagnostic agents requiring selective localization or delivery to areas of platelet mediated thrombus formation in an animal, including a human plant, and substituted for other binding proteins and/or **antibody**-based reagents in assay or diagnostic tests.
Dwg.0/0

L39 ANSWER 23 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-605694 [57] WPIDS
CROSS REFERENCE: 1998-467563 [40]; 1999-469134 [39]; 2000-181809 [16]; 2000-686027 [67]; 2003-138230 [13]; 2003-208759 [20]
DOC. NO. CPI: C2003-164816
TITLE: Novel conjugates comprising **antibody** fragments covalently attached to nonproteinaceous polymer molecules, useful for treating inflammatory diseases, acute lung injury, ischemic reperfusion injury, pneumonia and asthma.
DERWENT CLASS: A96 B04 C06 D16
INVENTOR(S): HSEI, V; KOUMENIS, I; LEONG, S; PRESTA, L; SHAHROKH, Z; ZAPATA, G
PATENT ASSIGNEE(S): (GETH) GENENTECH INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003021790	A1	20030130	(200357)*		266

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2003021790	A1	Provisional	US 1998-74330P	19980122
		Provisional	US 1998-75467P	19980220
		Provisional	US 1998-94003P	19980724
		Provisional	US 1998-94013P	19980724
		Cont of	US 1999-234182	19990120
			US 2000-726258	20001129

PRIORITY APPLN. INFO: US 2000-726258 20001129; US 1998-74330P 19980122; US 1998-75467P 19980220; US 1998-94003P 19980724; US 1998-94013P 19980724; US 1999-234182 19990120
AN 2003-605694 [57] WPIDS
CR 1998-467563 [40]; 1999-469134 [39]; 2000-181809 [16]; 2000-686027 [67]; 2003-138230 [13]; 2003-208759 [20]
AB US2003021790 A UPAB: 20030906
NOVELTY - A conjugate (I) comprising one or more **antibody** fragments covalently attached to one or more nonproteinaceous polymer molecules, where the apparent size of the conjugate is at least 500

kDa, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition (II) comprising (I) and a carrier.

ACTIVITY - Antiinflammatory; Vasotropic; Cardiant; Immunosuppressive; Antiulcer; Antibacterial, Antiasthmatic.

Full length murine anti-rabbit IL-8 monoclonal **antibody** 6G4.2.5, 20 kDa linear **PEG**-6G4V11N35E Fab', 30 kDa linear **PEG**-6G4V11N35E Fab', and 40 kDa branched **PEG**-6G4V11N35E Fab' were tested in a rabbit ear model of tissue ischemia and reperfusion injury. 1-1.5 kg New Zealand white rabbits were obtained from western Oregon rabbit company. General anesthesia was achieved by intramuscular injections of ketamin (50 mg/kg), xylazine (5 mg/kg) and acepromazine (2 mg/kg). The right external ear was prepared for surgery and under sterile procedure, the ear was transected at its base, leaving intact the central artery and vein. A straight microaneurysm clip was placed across the artery to produce complete ischemia. The ear was reattached with a clip exiting through the wound. The rabbits were then housed and later the clip was removed to effect reperfusion. Untreated rabbits received an intravenous injection of vehicle immediately prior to reperfusion. Treated animals received 5 mg/kg full length immunoglobulin (Ig) G murine anti-rabbit IL-8 monoclonal **antibody** 6G4.2.5, 20 CD linear **PEG**-6G4V11 N35E Fab', 30 kDa linear **PEG**-6G4V11N35E Fab' or 40 kDa branched **PEG**-6G4V11N35E Fab' immediately prior to reperfusion. The ear volume and necrosis were measured daily. Animals were sacrificed at day 1 and day 7 for histological evaluation of the ear and the same section of ear was taken from all animals. In the rabbit model of ear ischemia reperfusion injury, **antibody** was administered intravenously at a single dose at the prime of reperfusion. The ischemic reperfusion injury was characterized by tissue damage, edema, and sometimes necrosis. The resulting data showed that the treatment with 20 kDa linear **PEG**-, 30 kDa linear **PEG**- and 40 kDa branched **PEG**-conjugated Fab's effectively reduced ear swelling and edema at all time point of observation. The efficacy of all the 3 PEGylated Fab's were statistically indistinguishable from the full length IgG murine anti-rabbit L-8 monoclonal **antibody** 6G4.2.5 at all time points. These data supported the efficacy of large effective size anti-IL-8 Fab'-**PEG** conjugates in ischemic reperfusion injury.

MECHANISM OF ACTION - None given.

USE - (I) is useful for treating an interleukin (IL)-8 mediated disease or disorder, such as inflammatory diseases, ischemic reperfusion injury e.g. myocardial infarction, acute lung injury e.g. adult respiratory distress syndrome (ARDS), hypvolemic shock, inflammatory bowel disease e.g. ulcerative colitis, bacterial pneumonia, and asthma. (I) is also useful as a reagent in an animal model system for in vivo study of the biological functions of the antigen recognized by the conjugate.

Dwg.0/71

L39 ANSWER 24 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-040659 [03] WPIDS
DOC. NO. NON-CPI: N2003-031909
DOC. NO. CPI: C2003-009645
TITLE: New human monoclonal **antibodies** against Streptococcus pneumoniae capsular **polysaccharides**, useful for treating or preventing S. pneumoniae infections, e.g. pneumonia,

meningitis, bacteremia or chronic lymphocytic leukemia.

DERWENT CLASS: B04 D16 S03
INVENTOR(S): FASCHING, C; JANOFF, E N
PATENT ASSIGNEE(S): (FASC-I) FASCHING C; (JANO-I) JANOFF E N
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002079254	A1	20021010	(200303)*	EN	60

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

AU 2002254485	A1	20021015	(200432)
US 2004198960	A1	20041007	(200466)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002079254	A1		WO 2002-US10129	20020329
AU 2002254485	A1		AU 2002-254485	20020329
US 2004198960	A1	Provisional	US 2001-279918P	20010329
		Provisional	US 2001-286725P	20010425
			WO 2002-US10129	20020329
			US 2004-483447	20040107

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002254485	A1	Based on	WO 2002079254

PRIORITY APPLN. INFO: US 2001-286725P 20010425; US 2001-279918P 20010329; US 2004-483447 20040107

AN 2003-040659 [03] WPIDS

AB WO 200279254 A UPAB: 20030113

NOVELTY - A human monoclonal **antibody** or its antigen-binding fragments, which specifically binds to a capsular or cell-wall-associated **polysaccharide** antigen of Streptococcus pneumoniae, is new. The human monoclonal **antibody** consists of 1A01, 2A01, 2A02, 2A03, 2G01, 2A04, 3A01, 3G01, 4G01, 7A01, 8A01, 8A04, 8A02, 8G01, 9G01, 33G01, 18CA01, 22FG01, 6BG01, 6BA01 or CPSM01.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a hybridoma cell line comprising Z727 1D8 1C7 2B8, BBK040 1F2 1G7 2G8, Z531 3D7 5A9 1A9, Z531 4B6 3F5 1E2, Z727 1C11 1E12 3B10, Z727 1D11 1D11 1F6, Z531 1F9 3H9 1B7, Z727 2G6 1B5 3B7, Z727 2B5, Z727 1G8 1B10 3E1, 1A8 1A3/1F7/1H59, BBK038 2F4 F11 1B6, BBK040 1D9 2B5, BBK040 4E4 2D1 1A5, BBK038 1B8 E2 1F6, Z727 1G8 1B10 1E12/3D5, Z727 1C11 1F7 2A8, Z727 1G8 1B3 1B11/1F9, Z727 1D11 1H6, BBK040 4E4 1A2, Z727 1D11 1E7 2E1, or BBK041 2G5 1G2L;

(2) pharmaceutical compositions comprising:

(a) at least one the novel **antibodies** or its antigen-binding fragment; or

(b) a cocktail comprising the novel monoclonal **antibodies** or their antigen-binding fragments;

(3) detecting Streptococcus pneumoniae comprising contacting a biological sample with the novel **antibody**;

(4) a standard for use in a diagnostic immunoassay comprising at least one of the novel **antibodies**;

(5) treating or preventing a S. pneumoniae infection in an individual; and

(6) an anti-idiotypic **antibody** that specifically binds to the novel **antibody**.

ACTIVITY - Antibacterial; Antiinflammatory; Auditory; Antianemic; Antiviral; Anti-HIV (human immunodeficiency virus); Cytostatic.

32 mice were injected intraperitoneally with 2 micro g of monoclonal **antibody** or phosphate buffered saline (PBS), then intranasally inoculated with 2 multiply 107 S. pneumoniae Serotype 2. Results showed that more 50 % of mice survived when protected with the immunoglobulin (Ig)A human monoclonal **antibodies**. In contrast, control mice had a survival rate of less than 10 %.

MECHANISM OF ACTION - Capsular/Cell-wall-associated **Polysaccharide** Antagonist.

USE - The **antibody** or compositions are useful for treating or preventing a S. pneumoniae infection in an individual (e.g. a human patient, or an individual with an impaired ability to produce **antibodies**), e.g. pneumococcal pneumonia, meningitis, otitis media, sinusitis, sickle cell anemia, hypogammaglobulinemia, asplenia, bacteremia, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), functional or surgical asplenia, chronic lymphocytic leukemia (CLL), or multiple myeloma. The individual may also include a patient under two years of age or a patient who experiences recurrent meningitis because of a skull fracture or other structural defects. (All claimed).

Dwg.0/9

L39 ANSWER 25 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-599455 [64] WPIDS

DOC. NO. CPI: C2002-169286

TITLE: Producing bispecific molecule having first antigen recognition portion that binds C3b-like receptor and second antigen recognition portion binding pathogenic antigenic molecule by using protein transplicing technique.

DERWENT CLASS: B04 D16

INVENTOR(S): HIMAWAN, J

PATENT ASSIGNEE(S): (ELUS-N) ELUSYS THERAPEUTICS INC; (HIMA-I) HIMAWAN J

COUNTRY COUNT: 98

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002046208	A2	20020613	(200264)*	EN	109

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002041556 A 20020618 (200266)
EP 1339427 A2 20030903 (200365) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2004077842 A1 20040422 (200428)
JP 2004515233 W 20040527 (200435) 169

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002046208	A2	WO 2001-US45653	20011101
AU 2002041556	A	AU 2002-41556	20011101
EP 1339427	A2	EP 2001-988231	20011101
		WO 2001-US45653	20011101
US 2004077842	A1	WO 2001-US45653	20011101
		US 2003-415840	20031103
JP 2004515233	W	WO 2001-US45653	20011101
		JP 2002-547945	20011101

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002041556	A	Based on	WO 2002046208
EP 1339427	A2	Based on	WO 2002046208
JP 2004515233	W	Based on	WO 2002046208

PRIORITY APPLN. INFO: US 2000-244811P 20001101; US 2003-415840 20031103

AN 2002-599455 [64] WPIDS

AB WO 200246208 A UPAB: 20021007

NOVELTY - Producing (M1) bispecific molecule (I) having a first antigen recognition portion (A1) that binds a C3b-like receptor (R) and a second antigen recognition portion (A2) that binds a pathogenic antigenic molecule (M) by using protein transplicing technique.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing a polyclonal library of (I), each member of polyclonal library having A1 and A2 involves (M3-M4): (M3) contacting several A1 and A2 to produce polyclonal library of (I), where each of N-intein A1 comprises A1 conjugated to amino terminus of N-intein of split intein, and each of several C-intein A2 comprises A2 having different binding specificities conjugated to carboxy terminus of C-intein of split intein; or (M4) contacting a population of N-intein A1 and a population of C-intein streptavidin under conditions such that protein trans-splicing occurs to produce a population of A1-streptavidin molecule, where each of the several of C-intein streptavidin comprises core streptavidin conjugated to the carboxy terminus of a C-intein of the split intein; and contacting the population of A1 streptavidin molecule and several biotinylated A2, each having a different antigen recognition specificity under conditions conducive to binding between streptavidin and biotin, to produce the polyclonal library of bispecific molecules;

(2) producing a C-intein antigen recognition portion phage display library;

(3) (I) comprising A1 that binds to C3b-like receptor, and A2 that binds to pathogenic antigenic molecule, where A1 comprises a monoclonal **antibody**, and A2 is conjugated to a carboxy

terminus of a **heavy** or **light chain** of A1;

(4) (I) comprising A1 that binds a C3b-like receptor; a linker; and A2 that binds a pathogenic antigenic molecule; where A2 is conjugated to carboxy terminus of A1 by the linker;

(5) a polyclonal library (II) of (I) comprising several (I) as described above;

(6) a composition (III) comprising several purified (I), where each (I) comprises a different A2 that has different binding specificity;

(7) a molecule (IV) comprising an antigen recognition portion that binds a C3b-like receptor and N-intein moiety comprising an N-intein of split intein; where the antigen recognition portion is conjugated to the amino acid terminal end of the N-intein moiety;

(8) a molecule (V) comprising an antigen recognition portion and an C-intein moiety comprising an C-intein of split intein; where the antigen recognition portion is conjugated to the amino acid terminal end of the C-intein moiety;

(9) a molecule (VI) comprising streptavidin and C-intein of split intein comprising immediately at the C-terminal side of the splice junction, an amino acid residue such as **Cys**, Ser, or Thr, where streptavidin is conjugated to carboxy terminus of C-intein;

(10) a C-intein antigen recognition portion phage display library, comprising several phages, where each phage displays on its surface a different C-intein polypeptide fusion protein, where each polypeptide has a different binding specificity;

(11) an expression vector, comprising a transcriptional regulatory element operably linked to a nucleotide sequence;

(12) a nucleic acid encoding N-intein fused to carboxy terminus of **heavy** or **light chain** of an anti-CR1 monoclonal **antibody**, or Fc domain that is fused to a scFv;

(13) a nucleic acid encoding a C-intein fused to the amino terminus of a polypeptide that binds an antigen, or core streptavidin via an optional linker;

(14) an expression vector comprising transcriptional regulatory element operably linked to nucleotide sequence encoding C-intein fused to amino terminus of polypeptide or streptavidin as described above;

(15) several nucleic acids encoding several C-intein antigen recognition portions and several expression vectors each comprising transcriptional regulatory element operably linked to nucleotide sequence encoding C-intein antigen recognition portion;

(16) a kit comprising in one container (I), (IV), (V);

(17) a kit comprising in two containers (IV) and (V);

(18) a kit comprising in one or more containers a first vector and a second vector, the first vector comprising a first DNA sequence encoding a A1 fused to the amino terminus of an N-intein peptide comprising an N-intein of a split intein, the second vector comprising a second DNA sequence encoding a A2 fused to the carboxy terminus of a C-intein peptide comprising a C-intein of the split intein;

(19) a kit comprising in one or more containers a first vector and a second vector, the first vector comprising a first DNA sequence encoding a A1 fused to the amino terminus of an N-intein peptide comprising an N-intein of a split intein, the second vector comprising a second DNA sequence encoding core streptavidin fused to carboxy terminus of C-intein peptide comprising a C-intein of the split intein;

(20) a kit comprising a phage display library, where each phage displays a different C-intein polypeptide fusion protein on its surface; and

(21) a cell transformed with vector (V1) comprising DNA sequence encoding A1 fused to amino terminus of an N-intein of a split intein, vector (V2) comprising DNA sequence encoding A2 fused to carboxy terminus of C-intein of split intein, or vector (V3) comprising DNA sequence encoding core streptavidin fused to carboxy terminus of C-intein of the split intein, or V1 and V2; or containing A1 and/or A2 fused to amino terminus and carboxy terminus of N-intein and C-intein respectively.

ACTIVITY - Antibacterial; Antiparasitic; Immunosuppressive; Fungicide; Anti-HIV. No supporting data is given.

MECHANISM OF ACTION - Binds to hematopoietic cells expressing a C3b-like receptor on their surface and clears pathogenic antigen or autoantibody from circulation.

USE - For producing bispecific molecule having first antigen recognition portion that binds C3b-like receptor and second antigen recognition portion binding pathogenic antigenic molecule. (I) having A1 (preferably monoclonal **antibody**) and A2 is useful for treating or preventing a mammal, (a human or non-human mammal) having a disease or disorder or undesirable condition associated with the presence of a pathogen or pathogenic antigenic molecule. The pathogen may be an autoimmune agent, infectious agent, human immunodeficiency virus (HIV)-1, bacterium e.g., Bacillus anthracis, or fungus, parasite such as protozoan, or a toxin. (I) is also useful for treating a mammal having undesirable condition associated with the presence of pathogen or pathogenic antigenic molecule by ex vivo therapy (all claimed).

ADVANTAGE - The method for producing bispecific molecules using protein trans-splicing is site-specific, permitting the design and construction of bispecific molecules with particular structure and function(s).

Dwg.0/3

L39 ANSWER 26 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-138230 [13] WPIDS

CROSS REFERENCE: 1998-467563 [40]; 1999-469134 [39]; 2000-181809 [16]; 2000-686027 [67]; 2003-208759 [20]; 2003-605694 [57]

DOC. NO. CPI: C2003-035082

TITLE: Treating acute lung injury in mammal by administering to mammal a 500 kD conjugate comprising F(ab') 2 **antibody** fragment that binds to human interleukin-8, covalently attached to one or two **polyethylene** glycol molecules.

DERWENT CLASS: A25 A96 B04 D16

INVENTOR(S): HSEI, V; KOUMENIS, I; LEONG, S; PRESTA, L; SHAHROKH, Z; ZAPATA, G

PATENT ASSIGNEE(S): (GETH) GENENTECH INC

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6468532	B1	20021022	(200313)*		259

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6468532	B1 Provisional	US 1998-74330P	19980122
	Provisional	US 1998-75467P	19980220

Searcher : Shears 571-272-2528

Provisional	US 1998-94003P	19980724
Provisional	US 1998-94013P	19980724
	US 1999-234340	19990120

PRIORITY APPLN. INFO: US 1999-234340 19990120; US
1998-74330P 19980122; US
1998-75467P 19980220; US
1998-94003P 19980724; US
1998-94013P 19980724

AN 2003-138230 [13] WPIDS

CR 1998-467563 [40]; 1999-469134 [39]; 2000-181809 [16]; 2000-686027 [67]; 2003-208759 [20]; 2003-605694 [57]

AB US 6468532 B UPAB: 20030906

NOVELTY - Treating acute lung injury in a mammal by administering to the mammal a conjugate of a single **antibody** fragment (I) covalently attached to one or two **polyethylene** glycol (**PEG**) molecules, where (I) is F(ab')2 which comprises an antigen binding site that binds to human interleukin-8 (IL-8) and the size of the conjugate is at least about 500 kD.

DETAILED DESCRIPTION - Treating acute lung injury in a mammal, comprises administering to the mammal an effective amount of a conjugate of a single **antibody** fragment covalently attached to 1 or 2 **polyethylene** glycol (**PEG**) molecules, where the **antibody** fragment is a F(ab')2 comprising:

(a) first **chain** that is either a **light chain** or a **heavy chain**;

(b) a first opposite **chain** that is either a **heavy chain** opposite the first **light chain** or a **light chain** opposite the first **heavy chain**;

(c) a second **chain** that is either a **light chain** or a **heavy chain**; and

(d) a second opposite **chain** that is either a **heavy chain** opposite the second **light chain** or a **light chain** opposite the second **heavy chain**; where every **PEG** molecule is covalently attached to a first **cysteine** residue in the first or second chain that would ordinarily form a disulfide bridge with a second **cysteine** residue in the first or second opposite chain, where the disulfide bridge is avoided by substitution of another amino acid residue for the second **cysteine** residue in the first or second opposite chain, where the F(ab')2 comprises an antigen binding site that binds to human interleukin-8 (IL-8), and where the apparent size of the conjugate is at least about 500 kD.

ACTIVITY - Antiinflammatory; Respiratory.

A Fab'-SH **antibody** fragment of the affinity matured anti-IL-8 **antibody** 6G4V11N35E was expressed using the Fab' expression plasmid for 6G4V11N35E in Escherichia coli grown to high density in the fermentor. Anti-IL-8 6G4V11N35E Fab' variant was purified from fermentation paste and modified with 20 kD linear methoxy-**PEG**-maleimide. Pegylated material was formulated in phosphate buffered saline (PBS) at physiological pH. Full length 6G4.2.5 **antibody** was obtained from hybridoma cell line 6G4.2.5. Male New Zealand White rabbits weighing 2.2 to 2.5 kg were anesthetized. The abdominal area of the anesthetized animals were shaved and prepared for surgery. Via a midline laparotomy, the superior mesenteric artery (SMA) was isolated and a microvascular arterial clip applied at the aortic origin. Before the temporary

closure of the abdomen using 9 mm would clip, 15 ml of normal saline (38 deg. C) was given intraperitoneally. After 110 minutes of intestinal ischemia, the abdominal incision was reopened and the arterial clip was released to allow reperfusion. The laparotomy incision was closed in two layers. After surgery, the animals were placed on a heating pad continuously monitored for up to 6 hours post reperfusion. At 22-24 hr post-reperfusion, a tracheotomy was performed. Normal physiologic saline was diluted 1:3 with water and adjusted to pH 1.5 and 3 ml/kg body weight was then instilled intra-tracheally through an uncuffed tracheal tube. After instillation, the trachea was closed with 3-0 silk suture and the rabbits were allowed to recover. Rectal temperature was maintained at 37 deg. C +/-1 deg. C. Treated animals received an intravenous injection of 7 mg/kg 20 kD linear **PEG**-6G4V1135E Fab' at 10 minutes before and 6 hours after acid instillation. In the rabbit model of adult respiratory distress syndrome (ARDS), lung injury is manifested by hypoxemia lung edema and pro-inflammatory infiltrates into the alveolar space. Although 40 kD branched **PEG** -6G4V1135E Fab' did not protect rabbits from lung injury at any of the doses tried (5-20 mg/kg), the 20 kD linear **PEG**-6G4V11N35E Fab' had efficacy equal to, and, for some end-points, superior to that of the full length IgG murine anti-rabbit IL-8 monoclonal **antibody** 6G4.2.5 and prevented lung injury in the rabbits. These data indicated that large effective size anti-IL-8 Fab'-**PEG** conjugates acute lung injury and ARDS were effective.

MECHANISM OF ACTION - Inhibits IL-8 binding and activation of human neutrophils.

USE - The method is useful for treating lung injury, including adult respiratory distress syndrome (ARDS) in a mammal (claimed).

ADVANTAGE - (I) has an increased size than the conventional **antibody** fragment-polymer conjugates, and confers an increase in serum half-life, an increase in mean residence time in circulation, and/or a decrease in serum clearance rate over underivatized **antibodies**, and thus is a molecule with useful pharmacokinetic profile.

Dwg.0/71

L39 ANSWER 27 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER:	2003-208759 [20] WPIDS
CROSS REFERENCE:	1998-467563 [40]; 1999-469134 [39]; 2000-181809 [16]; 2000-686027 [67]; 2003-138230 [13]; 2003-605694 [57]
DOC. NO. CPI:	C2003-053000
TITLE:	Treating inflammatory disorder in a mammal, involves administering a conjugate of **polyethylene** glycol and a single **antibody** fragment comprising antigen binding site that binds to human interleukin-8, to mammal.
DERWENT CLASS:	A96 B04 D16
INVENTOR(S):	HSEI, V; KOUMENIS, I; LEONG, S; PRESTA, L; SHAHROKH, Z; ZAPATA, G
PATENT ASSIGNEE(S):	(GETH) GENENTECH INC
COUNTRY COUNT:	1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6458355	B1	20021001	(200320)*		259

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6458355	B1 Provisional	US 1998-74330P	19980122
	Provisional	US 1998-75467P	19980220
		US 1998-121952	19980724

PRIORITY APPLN. INFO: US 1998-121952 19980724; US 1998-74330P 19980122; US 1998-75467P 19980220

AN 2003-208759 [20] WPIDS

CR 1998-467563 [40]; 1999-469134 [39]; 2000-181809 [16]; 2000-686027 [67]; 2003-138230 [13]; 2003-605694 [57]

AB US 6458355 B UPAB: 20030906

NOVELTY - Treating (M) an inflammatory disorder in a mammal, comprising administering to the mammal, an effective amount of a conjugate (I) of a single **antibody** fragment (II) covalently attached to one or two **polyethylene** glycol (**PEG**) molecules, is new. (II) comprises an antigen binding site that binds to human interleukin-8 (IL-8), and the apparent size of (I) is at least 500 kDa.

DETAILED DESCRIPTION - Treating (M) an inflammatory disorder in a mammal, comprising administering to the mammal, an effective amount of a conjugate (I) of a single **antibody** fragment (II) covalently attached to 1 or 2 **polyethylene** glycol (**PEG**) molecules, where (II) is a F(ab')2 comprising a first **light** or **heavy chain**, a first opposite **chain** that is either a **heavy chain** opposite the first **light chain** or a **light chain** opposite the first **heavy chain**, a second **light** or **heavy chain** and a second opposite **chain** that is either a **heavy chain** opposite the second **light chain** or a **light chain** opposite the second **heavy chain**, is new. Every **PEG** molecule is covalently attached to a first **cysteine** residue in the first or second chain that would ordinarily form a disulfide bridge with a second **cysteine** residue in the first or second opposite chain, where the disulfide bridge is avoided by substitution of another amino acid residue for the second **cysteine** residue in the first or second opposite chain, where the F(ab')2 comprises an antigen binding site that binds to human IL-8, and the apparent size of (I) is at least 500 kDa.

ACTIVITY - Antiinflammatory; Vasotropic; Cardiant; Vulnerary; Antipsoriatic; Dermatological; Cerebroprotective; Neuroprotective; Ophthalmological; Osteopathic; Antiarthritic; Antirheumatic; Antibacterial; Hepatotropic; Antialcoholic; Virucide; Nephrotropic; Immunosuppressive; Antiulcer.

Full length murine anti-rabbit IL-8 monoclonal **antibody** 6G4.2.5, 20 kDa linear **PEG**-6G4V11N35E Fab', 30 kDa linear **PEG**-6G4V11N35E Fab' and 40 kDa linear **PEG**-6G4V1N35E Fab' were tested in a rabbit ear model of tissue ischemia and reperfusion injury. 1.0-1.5 kg New Zealand White rabbits were used. General anesthesia was achieved by intramuscular injections of Ketamine (50 mg/kg) plus Xylazine (5 mg/kg) and Acepromazine (2 mg/kg). The right external ear was prepared for surgery and under sterile procedure the ear was transected at its base, leaving intact only the central artery and vein. All nerves were transected to ensure

that the ear was completely anesthetic. A straight microaneurysm clip was placed across the artery to produce complete ischemia. The ear was reattached with the clip exiting through the wound. The rabbits were then housed at 26 deg. C and 6 hours later, the clip was removed to effect reperfusion. Untreated rabbits (n=11 animals) received an intravenous injection of vehicle (10 mM sodium acetate, 8 % trehalose and 0.01 % polysorbate-20 at pH 5.5) immediately prior to reperfusion. Treated animals received 5 mg/kg full length immunoglobulin (Ig)G murine anti-rabbit IL-8 monoclonal **antibody** 6G4.2.5 (n=4 animals), 20 kDa linear **PEG**-6G4V11N35E Fab'(n=3 animals), 30 kDa linear **PEG**-6G4V11N35E Fab' (n=3 animals), or 40 kDa linear **PEG**-6G4V1N35E Fab' (n=3 animals) immediately prior to reperfusion. The ear volume and necrosis were measured daily by procedures described in Vedder et al. supra. Animals were sacrificed at days 1 and 7 for histological evaluation of the ear and the same section of the ear was taken from all animals. To determine the therapeutic agents did not adversely affect any hematological parameter, aliquots of blood were withdrawn for complete blood counts and differentials immediately before reperfusion, and at 24 hour intervals. In a separate experiment, blood samples were taken at 1,5,15 and 30 minutes, and at 1 hour and 4 hours. The results showed that treatment with 20 kDa linear **PEG**-, 30 kDa linear **PEG**- and 40 kDa-linear **PEG**- branched **PEG** -conjugated FAb's effectively reduced ear swelling and edema at all time points of observations (days 1,3 and 5). In fact, the efficacy of all three PEGylated Fab's was statistically indistinguishable from that of the full length IgG murine anti-rabbit IL-8 monoclonal **antibody** 6G4.2.5. at all time points observed. The data supported the efficacy of large effective size anti-IL-8 Fab'-**PEG** conjugates in ischemic reperfusion injury and specifically support the ability of 40 kDa branched **PEG**-conjugated Fab' molecules to reach and act on disease effector targets in circulation and other tissues.

MECHANISM OF ACTION - Vaccine.

USE - (M) is useful for treating an inflammatory disorder e.g. ischemic reperfusion disorder such as surgical tissue reperfusion injury, myocardial ischemia or myocardial infarction, or hypovolemic shock, in a mammal e.g. human (claimed). The method is useful for treating inflammatory disorders including psoriasis, atopic dermatitis, systemic scleroderma and sclerosis, responses associated with inflammatory bowel disease, ischemic reperfusion disorders, myocardial ischemic conditions, cerebral edema secondary to stroke, cranial trauma, asphyxia, adult respiratory distress syndrome, acute-lung injury, Behcet's disease, dermatomyositis, polymyositis, multiple sclerosis, dermatitis, meningitis, encephalitis, uveitis, osteoarthritis, lupus nephritis, autoimmune diseases such as rheumatoid arthritis, Sjogren's syndrome, vasculitis, central nervous system inflammatory disorder, multiple organ injury syndrome secondary to septicemia or trauma, alcoholic hepatitis, bacterial pneumonia, antigen-**antibody** complex mediated diseases including glomerulonephritis, sepsis, sarcoidosis, immunopathologic responses to tissue/organ transplantation, inflammations of the lung, and inflammatory bowel disease such as ulcerative colitis.

Dwg.0/71

L39 ANSWER 28 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-216732 [27] WPIDS
DOC. NO. CPI: C2002-066152
TITLE: New **antibody** specific for human tumor

necrosis factor (TNF)-alpha, useful for treating TNF-alpha-mediated diseases, e.g. congestive heart failure, septic or endotoxic shock, cachexia, adult respiratory distress syndrome.

DERWENT CLASS: A96 B04 D16

INVENTOR(S): ATHWAL, D S; BROWN, D T; CHAPMAN, A P; KING, D J; POPPLEWELL, A G; WEIR, A N C; WEIR, A N; POPPLEVELL, A G; CHARLES WEIR, A N

PATENT ASSIGNEE(S): (CLLT) CELLTECH R & D LTD; (ATHW-I) ATHWAL D S; (BROW-I) BROWN D T; (CHAP-I) CHAPMAN A P; (WEIR-I) CHARLES WEIR A N; (KING-I) KING D J; (POPP-I) POPPLEWELL A G; (WEIR-I) WEIR A N C

COUNTRY COUNT: 97

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001094585	A1	20011213	(200227)*	EN	119
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
GB 2366800	A	20020320	(200227)		
AU 2001060511	A	20011217	(200229)		
NO 2002000554	A	20020408	(200236)		
BR 2001006682	A	20020514	(200240)		
CZ 2002000837	A3	20020515	(200241)		
SK 2002000315	A3	20020702	(200253)		
US 2002151682	A1	20021017	(200270)		
HU 2002002346	A2	20021028	(200277)		
KR 2002047097	A	20020621	(200280)		
US 2003026805	A1	20030206	(200313)		
EP 1287140	A1	20030305	(200319)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
CN 1383450	A	20021204	(200322)		
ZA 2002000097	A	20030326	(200327)		121
DE 10192353	T	20030522	(200335)		
JP 2003535591	W	20031202	(200382)		127
NZ 516596	A	20040730	(200454)		
MX 2001013440	A1	20030901	(200465)		
GB 2366800	B	20050119	(200506)		
ES 2230975	A1	20050501	(200530)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001094585	A1	WO 2001-GB2477	20010605
GB 2366800	A	WO 2001-GB2477	20010605
		GB 2001-28386	20011127
AU 2001060511	A	AU 2001-60511	20010605
NO 2002000554	A	WO 2001-GB2477	20010605
		NO 2002-554	20020204
BR 2001006682	A	BR 2001-6682	20010605
		WO 2001-GB2477	20010605

CZ 2002000837	A3		WO 2001-GB2477	20010605
			CZ 2002-837	20010605
SK 2002000315	A3		WO 2001-GB2477	20010605
			SK 2002-315	20010605
US 2002151682	A1		US 2001-949559	20010910
		Cont of	US 2001-875221	20011018
HU 2002002346	A2		WO 2001-GB2477	20010605
			HU 2002-2346	20010605
KR 2002047097	A		KR 2002-701131	20020126
US 2003026805	A1		US 2001-875221	20011018
EP 1287140	A1		EP 2001-934209	20010605
			WO 2001-GB2477	20010605
CN 1383450	A		CN 2001-801629	20010605
ZA 2002000097	A		ZA 2002-97	20020104
DE 10192353	T		DE 2001-10192353	20010605
			WO 2001-GB2477	20010605
JP 2003535591	W		WO 2001-GB2477	20010605
			JP 2002-502126	20010605
NZ 516596	A		NZ 2001-516596	20010605
			WO 2001-GB2477	20010605
MX 2001013440	A1		WO 2001-GB2477	20010605
			MX 2001-13440	20011219
GB 2366800	B		GB 2001-28386	20010605
			WO 2001-GB2477	20010605
ES 2230975	A1		ES 2002-50012	20010605

FILING DETAILS:

PATENT NO	KIND		PATENT NO
GB 2366800	A	Based on	WO 2001094585
AU 2001060511	A	Based on	WO 2001094585
BR 2001006682	A	Based on	WO 2001094585
CZ 2002000837	A3	Based on	WO 2001094585
SK 2002000315	A3	Based on	WO 2001094585
HU 2002002346	A2	Based on	WO 2001094585
EP 1287140	A1	Based on	WO 2001094585
DE 10192353	T	Based on	WO 2001094585
JP 2003535591	W	Based on	WO 2001094585
NZ 516596	A	Based on	WO 2001094585
MX 2001013440	A1	Based on	WO 2001094585
GB 2366800	B	Based on	WO 2001094585

PRIORITY APPLN. INFO: GB 2000-13810 20000606
AN 2002-216732 [27] WPIDS
AB WO 200194585 A UPAB: 20050128
NOVELTY - An **antibody** molecule having specificity for human tumor necrosis factor-alpha (TNF alpha), comprising a **heavy** or **light chain**, is new.

DETAILED DESCRIPTION - An **antibody** molecule having specificity for human tumor necrosis factor-alpha (TNF alpha), comprising a **heavy** or **light chain**, is new. The variable domain of the **heavy chain** comprises a complementarily determining region (CDR) having the sequence given as H1 (AspTyrGlyMetAsn) for CDRH1, as H2' (TrpIleAsnThrTyrIleGlyGluProIleTyrAlaAspSerValLysGly), or as H2' (TrpIleAsnThrTyrIleGlyGluProIleTyrValAspAspPheLysGly) for CDRH2, or as H3 (GlyTyrArgSerTyrAlaMetAspTyr) for CDRH3. The variable domain of the **light chain** comprises a CDR having the sequence

given as L1 in (LysAlaSerGlnAsnValGlyThrAsnValAla) for CDRL1, as L2 (SerAlaSerPheLeuTyrSer) for CDRL2, or as L3 (GlnGlnTyrAsnIleTyrProLeuThr) for CDRL3.

INDEPENDENT CLAIMS are also included for the following:

(1) **antibody** molecules having specificity for human TNF alpha , having a **light** and **heavy chain** comprising a 214 or 229 residue amino acid sequence, respectively, both fully defined in the specification;

(2) a variant of the **antibody** molecule of (1) having an improved affinity for TNF alpha ;

(3) compounds comprising the **antibody** molecule which:

(a) is covalently attached to an amino acid at or towards the C-terminal end of its **heavy chain**, an effector or reporter molecule;

(b) is attached to one of the **cysteine** residues at the C-terminal end of the **heavy chain**, a lysyl-maleimide group where each amino group of the lysyl residue has covalently linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of 20000 Da; or

(c) has one or more synthetic or naturally occurring polymers attached to one of the **cysteine** residues at the C-terminal end of the **heavy chain**;

(4) an **antibody** molecule comprising a hybrid CDR having a truncated donor CDR sequence, where the missing portion of the donor CDR is replaced by a different sequence and forms a functional CDR;

(5) a DNA sequence which encodes the **heavy** and/or **light chain** of the **antibody** molecule;

(6) cloning or expression vector containing the DNA sequence, where vector is pDNAbEng-G1 or pTTO(CDP870);

(7) a host cell transformed with the vector of (6);

(8) a process of producing the **antibody** molecule by culturing the host cell of (7) and isolating the **antibody** molecule;

(9) a therapeutic or diagnostic composition comprising the **antibody** molecule or the compound comprising the **antibody**;

(10) a polypeptide having the sequence (S1).

(S1) is AspTyrGlyMetAsn, TrpIleAsnThrTyrIleGlyGluProIleTyrAlaAspSerValLysGly, GlyTyrArgSerTyrAlaMetAspTyr, LysAlaSerGlnAsnValGlyThrAsnValAla, SerAlaSerPheLeuTyrSer, GlnGlnTyrAsnIleTyrProLeuThr, or TrpIleAsnThrTyrIleGlyGluProIleTyrValAspAspPheLysGly.

ACTIVITY - Antirheumatic; antiarthritic; osteopathic; cardiant; anti-HIV (human immunodeficiency virus); antibacterial; immunosuppressive; antiallergic; antipsoriatic; tuberculostatic; immunomodulator; anti-inflammatory; vulnerary.

No biological data is given.

MECHANISM OF ACTION - TNF-Antagonist-Alpha.

USE - The **antibody** or the compound comprising the **antibody** is useful for treating or manufacturing a medicament for treating a pathology mediated by TNF alpha , such as rheumatoid- or osteo-arthritis (claimed). TNF alpha -mediated diseases which can be treated by the **antibody** include sepsis, congestive heart failure, septic or endotoxic shock, cachexia, adult respiratory distress syndrome, acquired immunodeficiency syndrome (AIDS), allergies, psoriasis, tuberculosis, inflammatory bone disorders, blood coagulation disorders, burns, rejection episodes following organ or tissue transplant, Crohn's disease, and autoimmune diseases, such as thyroiditis. The **antibodies** may also be used to reduce the

side effects associated with TNF alpha generation during neoplasty therapy, to eliminate or reduce shock-related symptoms associated with the treatment or prevention of graft rejection by use of an anti-lymphocyte **antibody**, for treating multi-organ failure, or in the diagnosis and imaging of disease states involving elevated levels of TNF alpha .
Dwg.0/24

L39 ANSWER 29 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-040075 [05] WPIDS
CROSS REFERENCE: 1993-303476 [38]; 1999-571244 [48]
DOC. NO. CPI: C2002-011361
TITLE: Pathogen-targeted biocatalyst for preventing or treating microbial infections comprises a binding agent and a catalytic group that degrades a component of the pathogen such that the pathogenecity is abrogated.
DERWENT CLASS: A89 B04 D16 J04
INVENTOR(S): CREA, R
PATENT ASSIGNEE(S): (CREA-I) CREA R
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6287561	B1	20010911	(200205)*		34

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6287561	B1	CIP of	US 1992-847800	19920306
		CIP of	US 1994-184635	19940118
		Cont of	US 1995-558269	19951113
			US 1999-410882	19991004

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6287561	B1	Cont of	US 5961973

PRIORITY APPLN. INFO: US 1995-558269 19951113; US 1992-847800 19920306; US 1994-184635 19940118; US 1999-410882 19991004
AN 2002-040075 [05] WPIDS
CR 1993-303476 [38]; 1999-571244 [48]
AB US 6287561 B UPAB: 20020123
NOVELTY - A pathogen-targeted biocatalyst comprising a binding agent which specifically binds a surface component of the pathogen and a catalytic group which degrades a component of the pathogen such that the pathogenecity is abrogated, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a virus targeted catalyst comprising a binding agent specific for a surface component of the virus and an enzyme, or its catalytically-active fragment, which degrades a surface component sufficiently to abrogate viral pathogenecity;

(2) a human immunodeficiency virus (HIV)-1-targeted biocatalyst, comprising a binding agent specific for gp120 coupled to a protease, or its catalytically-active fragment, which degrades gp120 sufficiently to abrogate viral pathogenecity;

(3) a hybrid DNA encoding the pathogen-targeted biocatalyst, comprising DNA encoding a binding agent that specifically binds a surface component of the pathogen and DNA encoding a catalytic group which degrades a component of the pathogen such that pathogenecity is abrogated; and

(4) a biocatalyst targeted to HIV comprising a fusion protein having a fully defined sequence of 383 or 376 amino acids, given in the specification or its functional portion, or a protein having substantial homology to the given sequences.

ACTIVITY - Virucide; antimicrobial.

MECHANISM OF ACTION - Biocatalyst.

USE - The biocatalysts are useful for preventing or treating infections by pathogenic microorganisms. These are specifically targeted to bind pathogens and to degrade components of pathogens to abrogate their pathogenecity. The biocatalysts are particularly useful in the treatment of human immunodeficiency virus (HIV).

Dwg.0/11

L39 ANSWER 30 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-126459 [11] WPIDS
DOC. NO. CPI: C2000-038477
TITLE: A divalent **antibody** fragment useful in the treatment and diagnosis of tumors.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): CHAPMAN, A P; KING, D J
PATENT ASSIGNEE(S): (CLLT) CELLTECH THERAPEUTICS LTD
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9964460	A1	19991216	(200011)*	EN	43
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9942783	A	19991230	(200022)		
GB 2354242	A	20010321	(200117)		
EP 1090037	A1	20010411	(200121)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 19983347	T	20010628	(200138)		
JP 2002517515	W	20020618	(200242)		49
AU 763246	B	20030717	(200356)		
GB 2354242	B	20031105	(200377)		
EP 1090037	B1	20041117	(200476)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 69922003	E	20041223	(200501)		
ES 2232185	T3	20050516	(200535)		
DE 69922003	T2	20051201	(200579)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 9964460	A1	WO 1999-GB1800	19990608
AU 9942783	A	AU 1999-42783	19990608
GB 2354242	A	WO 1999-GB1800	19990608
		GB 2000-30176	20001211
EP 1090037	A1	EP 1999-955481	19990608
		WO 1999-GB1800	19990608
DE 19983347	T	DE 1999-1083347	19990608
		WO 1999-GB1800	19990608
JP 2002517515	W	WO 1999-GB1800	19990608
		JP 2000-553466	19990608
AU 763246	B	AU 1999-42783	19990608
GB 2354242	B	WO 1999-GB1800	19990608
		GB 2000-30176	20001211
EP 1090037	B1	EP 1999-955481	19990608
		WO 1999-GB1800	19990608
DE 69922003	E	DE 1999-622003	19990608
		EP 1999-955481	19990608
		WO 1999-GB1800	19990608
ES 2232185	T3	EP 1999-955481	19990608
DE 69922003	T2	DE 1999-622003	19990608
		EP 1999-955481	19990608
		WO 1999-GB1800	19990608

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9942783	A	Based on	WO 9964460
GB 2354242	A	Based on	WO 9964460
EP 1090037	A1	Based on	WO 9964460
DE 19983347	T	Based on	WO 9964460
JP 2002517515	W	Based on	WO 9964460
AU 763246	B	Previous Publ.	AU 9942783
		Based on	WO 9964460
GB 2354242	B	Based on	WO 9964460
EP 1090037	B1	Based on	WO 9964460
DE 69922003	E	Based on	EP 1090037
		Based on	WO 9964460
ES 2232185	T3	Based on	EP 1090037
DE 69922003	T2	Based on	EP 1090037
		Based on	WO 9964460

PRIORITY APPLN. INFO: GB 1998-12545 19980610

AN 2000-126459 [11] WPIDS

AB WO 9964460 A UPAB: 20000301

NOVELTY - A divalent **antibody** fragment comprising two **antibody heavy chains** and at least one polymer molecule in covalent linkage is new.

DETAILED DESCRIPTION - A divalent **antibody** fragment comprises two **antibody heavy chains** and at least one polymer molecule in covalent linkage. Each **heavy chain** being covalently linked to the other by at least one non-disulphide interchain bridge linking the sulfur atom of a **cysteine** residue in one chain to the sulphur atom of a **cysteine** residue in the other chain. The **cysteine** residues is located outside of the variable region domain of each chain. At least one non-disulphide interchain bridge contains a covalently linked polymer molecule.

An INDEPENDENT CLAIM is also included for a composition comprising an **antibody** fragment according to any of the preceding claims together with one or more excipients, diluents or carriers.

USE - The **antibodies** are useful for diagnostic and therapeutic purposes especially for tumor treatment and diagnosis.

Dwg.0/9

L39 ANSWER 31 OF 39 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-024034 [02] WPIDS
CROSS REFERENCE: 1999-080758 [07]; 2004-201266 [19]; 2005-201775 [21]
DOC. NO. NON-CPI: N1999-018498
DOC. NO. CPI: C1999-007292
TITLE: Conjugate of **polyalkylene** oxide with single chain antigen-binding peptide - used for detecting antigens, targetted drug delivery, imaging and affinity purification, has reduced antigenicity and immunogenicity but prolonged circulation time, and related nucleic acid.
DERWENT CLASS: A25 A96 B04 D16 S03
INVENTOR(S): FILPULA, D R; LEE, L S; SHORR, R G L; WHITLOW, M; WHITLOW, M D
PATENT ASSIGNEE(S): (ENZO-N) ENZON INC; (FILP-I) FILPULA D R; (LEEL-I) LEE L S; (SHOR-I) SHORR R G L; (WHIT-I) WHITLOW M
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9848837	A1	19981105	(199902)*	EN	116
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9872666	A	19981124	(199914)		
EP 979102	A1	20000216	(200014)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002505574	W	20020219	(200216)		110
US 2002061307	A1	20020523	(200239)		
US 2002098192	A1	20020725	(200254)		
US 6824782	B2	20041130	(200479)		
US 2005008650	A1	20050113	(200506)		
US 2005048064	A1	20050303	(200517)		
US 6872393	B2	20050329	(200522)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9848837	A1		WO 1998-US8654	19980430
AU 9872666	A		AU 1998-72666	19980430
EP 979102	A1		EP 1998-920001	19980430
			WO 1998-US8654	19980430
JP 2002505574	W		JP 1998-547347	19980430
			WO 1998-US8654	19980430
US 2002061307	A1	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623

Searcher : Shears 571-272-2528

		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
			US 2001-791578	20010226
US 2002098192	A1	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
			US 2001-791540	20010226
US 6824782	B2	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
			US 2001-791540	20010226
US 2005008650	A1	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
		Div ex	US 2001-791540	20010226
			US 2004-915069	20040810
US 2005048064	A1	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
		Div ex	US 2001-791578	20010226
			US 2004-909948	20040802
US 6872393	B2	Provisional	US 1997-44449P	19970430
		Provisional	US 1997-50472P	19970623
		Provisional	US 1997-63074P	19971027
		Provisional	US 1997-67341P	19971202
		Cont of	US 1998-69842	19980430
			US 2001-791578	20010226

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9872666	A Based on	WO 9848837
EP 979102	A1 Based on	WO 9848837
JP 2002505574	W Based on	WO 9848837

PRIORITY APPLN. INFO: US 1997-67341P 19971202; US 1997-44449P 19970430; US 1997-50472P 19970623; US 1997-63074P 19971027; US 1998-69842 19980430; US 2001-791578 20010226; US 2001-791540 20010226; US 2004-915069 20040810; US 2004-909948 20040802

AN 1999-024034 [02] WPIDS

CR 1999-080758 [07]; 2004-201266 [19]; 2005-201775 [21]

AB WO 9848837 A UPAB: 20050406

New conjugate (A) comprises (i) a **polyalkylene** oxide (PAO) and (ii) a single-chain antigen-binding polypeptide (I) consisting of

two polypeptides (II), each containing the antigen-binding part of the variable region of an **antibody heavy** or **light chain**, joined by a peptide linker (III). (A) has antigen-binding affinity 1-10 times that of (II) in unconjugated form.

Also new are:

(1) (II) that can be conjugated to PAO through **Cys** or Lys residues;

(2) nucleic acid (IV) encoding (II);

(3) cloning and expression vector containing (IV);

(4) host cells transformed with (IV);

(5) multivalent conjugate (A') containing PAO plus two or more (I).

USE - (A) are used (i) to detect specific antigens, for diagnosis or monitoring of disease, also for analysis of environmental samples, cell cultures, fermentation broths etc.; (ii) for targeted delivery of therapeutic, prophylactic or diagnostic agents, e.g. hormones, growth stimulators/inhibitors, pro-drug activating enzymes etc., or for treatment of cancer, infections, etc., (iii) in affinity purification and biosensors and (iv) when labelled, for imaging internal structures in animals. Cells of (4) are used to produce (II).

ADVANTAGE - Conjugation to PAO reduces immunogenicity and antigenicity, and increases half-life in the circulation, while retaining antigen-binding specificity and affinity. Many labels can be attached to a single (A), so sensitivity of immunoassays and histological tests is improved. Since drugs are (partly) detoxified when conjugated to (A), in the serum, side effects of the drug are reduced or larger doses may be given.

Dwg.5/8

L39 ANSWER 32 OF 39 MEDLINE on STN

ACCESSION NUMBER: 95249604 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7732025
TITLE: Peptide mimicry of the meningococcal group C capsular **polysaccharide**.
AUTHOR: Westerink M A; Giardina P C; Apicella M A; Kieber-Emmons T
CORPORATE SOURCE: Department of Medicine, Medical College of Ohio, Toledo 43699, USA.
CONTRACT NUMBER: AI26279 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995 Apr 25) 92 (9) 4021-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950608
Last Updated on STN: 20000303
Entered Medline: 19950601

AB Sequence analysis of the variable regions of the **heavy** and **light chains** of the anti-idiotypic **antibody** 6F9, which mimics the meningococcal group C capsular **polysaccharide** (MCP), was performed. The immunogenic site on 6F9 responsible for inducing an anti-MCP **antibody** response was determined by means of sequence and computer model analysis of these data. Complementarity-determining region 3 (CDR3) was found to be unique in that the sequence tract YRY was exposed on the surface.

A synthetic peptide spanning the CDR3 domain was synthesized and complexed to proteosomes (meningococcal group B outer membrane protein). Immunizations of BALB/c mice with the peptide-proteosome complex resulted in a significant anti-MCP **antibody** response. Immunized mice were protected against infection with a lethal dose of Neisseria meningitidis serogroup C.

L39 ANSWER 33 OF 39 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 96087058 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7488620
TITLE: A novel strategy affords high-yield coupling of **antibody** Fab' fragments to liposomes.
AUTHOR: Shahinian S; Silvius J R
CORPORATE SOURCE: Department of Biochemistry, McGill University, Montreal, Quebec, Canada.
SOURCE: Biochimica et biophysica acta, (1995 Nov 1) 1239 (2) 157-67.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960125
Last Updated on STN: 19960125
Entered Medline: 19960104

AB A new assay for the production of reactive sulfhydryl-bearing **antibody** Fab' fragments has been utilized to develop conditions affording high efficiencies of coupling of mouse and rabbit IgG-derived Fab' fragments to lipid vesicles containing maleimidyl-functionalized phospholipids. **Cysteine** and mercaptoethylamine, but not dithiothreitol, reduce **antibody** F(ab')2 to Fab' fragments in very good yields under conditions where overreduction to **heavy** and **light chains** is minimized. Surprisingly, however, a large fraction of the Fab' fragments generated under these conditions can lack maleimide-reactive sulfhydryl groups, as demonstrated using a maleimidyl-**poly**(**ethylene** glycol) conjugate to shift selectively the electrophoretic mobility of the reactive sulfhydryl-bearing Fab' fragments. After modification of F(ab')2 reduction conditions specifically to maximize the yield of the latter fraction, it is possible to achieve high and very reproducible coupling of functional Fab' fragments to liposomes (equivalent to coupling of ca. 70% of total input protein and almost 100% of the reactive sulfhydryl-bearing Fab' fraction). A novel phospholipid-**poly**(**ethylene** glycol)-maleimide 'anchor' allows particularly efficient coupling of Fab' fragments to liposomes, even using relatively low liposome concentrations and molar percentages of the liposome-incorporated 'anchor' species. These results demonstrate that with appropriate optimization of the conditions for Fab' production and liposome coupling, Fab' fragments can be coupled to liposomes with efficiencies comparable to or exceeding those reported for coupling of intact **antibodies**. These results should facilitate the wider use of Fab' fragments as a potentially advantageous alternative to intact **antibodies** for liposomal targeting in various applications.

L39 ANSWER 34 OF 39 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:421291 SCISEARCH

THE GENUINE ARTICLE: FY214
TITLE: THE KALLIKREIN-KININ SYSTEM IN THE RAT HYPOTHALAMUS - IMMUNOHISTOCHEMICAL LOCALIZATION OF HIGH-MOLECULAR-WEIGHT KININOGEN AND T-KININOGEN IN DIFFERENT NEURONAL SYSTEMS
AUTHOR: RICHOUX J P (Reprint); GELLY J L; BOUHNIK J; BAUSSANT T; ALHENCGELAS F; GRIGNON G; CORVOL P
CORPORATE SOURCE: FAC MED VANDOEUVRE NANCY, HISTOL EMBRYOL LAB, BP 184, F-54505 VANDOEUVRE NANCY, FRANCE (Reprint); INSERM, INSERM, U36, F-75005 PARIS, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: HISTOCHEMISTRY, (1991) Vol. 96, No. 3, pp. 229-243. ISSN: 0301-5564.
PUBLISHER: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 93
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB High molecular weight kininogen (HKg) and T kininogen (TKg) were detected and localized by immunocytochemistry in adult rat hypothalamus. In addition, kininogens were measured by their direct radioimmunoassay (RIA) or by indirect estimation of kinins released after trypsin hydrolysis and high pressure liquid chromatography (HPLC) separation of bradykinin (BK) and T kinin. A specific HKg immunoreactivity demonstrated with **antibodies** directed against the **light chain** (LC) of HKg was colocated with SRIF in neurons of hypothalamic periventricular area (**PVA**) projecting to external zone (ZE) of median eminence (ME). **Heavy chain** (HC) immunoreactivity which could be related to HKg or to low molecular weight kininogen (LKg) was detected in some other systems: i) parvocellular neurons of suprachiasmatic (SCN) and arcuate nuclei containing SRIF, ii) magnocellular neurons (mostly oxytocinergic) of paraventricular (PVN) and supraoptic (SON) nuclei, iii) neurons of dorsomedian and lateral hypothalamic areas. TKg immunostaining was restricted to magnocellular neurons of PVN, SON, accessory nuclei (mostly vasopressinergic) and to parvocellular neurons of SCN (vasopressinergic). TKg projections are directed towards the internal zone (ZI) of ME, but very few immunoreactive terminals are detectable in neurohypophysis. TKg staining parallels with vasopressin during water deprivation, and is undetectable in homozygous Brattleboro rats. In some magnocellular neurons, TKg and HC (related to HKg or LKg) are coexpressed. TKg, was also detected in hypothalamus and cerebellum extracts by direct RIA, and BK and T kinin were identified after trypsin hydrolysis. HKg and LKg can act as precursor of BK which can play a physiological role as releasing factor, neuromodulator - neurotransmitter, - or modulator of local microcirculation in hypothalamus. The three kininogens are also potent thiolprotease inhibitors which could modulate both the maturation processes of peptidic hormones and their inactivation and catabolism.

L39 ANSWER 35 OF 39 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 83256427 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6409088
TITLE: A new isotype sequence (V kappa 27) of the variable region of kappa-**light chains** from a

mouse hybridoma-derived anti-(streptococcal group A **polysaccharide**) **antibody** containing an additional **cysteine** residue. Application of the dimethylaminoazobenzene isothiocyanate technique for the isolation of peptides.
AUTHOR: Chang J Y; Herbst H; Aebersold R; Braun D G
SOURCE: Biochemical journal, (1983 Apr 1) 211 (1) 173-80. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198308
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19830811

AB The first complete sequence of the variable region of a kappa-**light chain** (V kappa) from a mouse anti-(streptococcal group A **polysaccharide**) **antibody** (immunoglobulin 7S34.1) is reported. Immunoglobulin 7S34.1 was isolated from the ascitic fluid of hybridoma 7S34.1 previously cloned in vitro. A newly developed technique for the isolation of peptides by using pre-column formation of peptide derivatives with dimethylaminoazobenzene isothiocyanate also served to complete the sequence. The sequence of the variable region of the kappa-**light chain** of immunoglobulin 7S34.1 defines a new mouse V kappa isotype (V kappa 27) and is the first mouse immunoglobulin **light-chain** variable region to be shown to have an extra **cysteine** residue at position 48.

L39 ANSWER 36 OF 39 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 83256426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6409087
TITLE: A new method for the selective isolation of **cysteine**-containing peptides. Specific labelling of the thiol group with a hydrophobic chromophore.
AUTHOR: Chang J Y; Knecht R; Braun D G
SOURCE: Biochemical journal, (1983 Apr 1) 211 (1) 163-71. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198308
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 20000303
Entered Medline: 19830811

AB A new method for the selective isolation of **cysteine**-containing peptides was designed. The method is based on the specific labelling of thiol groups with a hydrophobic chromophore followed by enzymic fragmentation of the labelled protein and reversed-phase high-pressure liquid-chromatographic separation of the peptide mixture. This new method has several distinct advantages: (1) the hydrophobic-chromophore-labelled **cysteine**-containing peptides are easily separated from non-**cysteine**-containing peptides by reversed-phase high-pressure liquid chromatography; (2) only **cysteine**-containing peptides are detected in the visible region with sensitivity at the low picomole level; this high

sensitivity allows isolation of nanogram amounts of pure **cysteine**-containing peptide; (3) during sequence determination of the chromophore-labelled **cysteine**-containing peptides, the **cysteine** residues are released as coloured anilinothiazolinone derivatives and can be detected directly in the picomole range; (4) with proteins bearing several disulphide groups, each disulphide group may undergo a different degree of reduction, and therefore the recovery of individual **cysteine**-containing peptides may be used to deduce the disulphide linkages present in the native protein. Two thiol-specific reagents, 4-dimethylaminoazobenzene-4'-iodoacetamide and 4-dimethylaminoazobenzene-4'-N-maleimide, were synthesized and characterized. The method was successfully used to isolate five **cysteine**-containing peptides from a completely reduced monoclonal-**antibody** kappa-**light chain** raised against the azobenzenearsonate determinant and six **cysteine**-containing peptides from a kappa-**light chain** raised against streptococcal group A **polysaccharide**. The principle of this method is applicable to the isolation of any peptide containing amino acid residues that can be specifically labelled with a hydrophobic chromophore.

L39 ANSWER 37 OF 39 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 81000289 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6157405
TITLE: Isolation of an active **heavy-chain** variable domain from a homogeneous rabbit **antibody** by cathepsin B digestion of the aminoethylated **heavy chain**.
AUTHOR: Ehrlich P H; Matsueda G R; Margolies M N; Husain S S; Haber E
CONTRACT NUMBER: CA-24432 (NCI)
HL-07208 (NHLBI)
HL-19259 (NHLBI)
SOURCE: Biochemistry, (1980 Aug 19) 19 (17) 4091-6.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198011
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19801125

AB Cathepsin B from bovine liver has been used to cleave the **heavy chain** of partially reduced and aminoethylated rabbit allotype a1 IgG. Three major cleavages have been identified, one of which appears to be at the peptide bond carboxy terminal to the two adjacent (aminoethyl)**cysteine** residues at positions 133 and 134. The variable domain of the **heavy chain** (**VH**) was isolated by gel filtration from both pooled heterogeneous rabbit IgG and a homogenous rabbit antitype III pneumococcal **polysaccharide antibody**. This VH inhibited the binding of 125I-labeled (allotype a) IgG to anti-a1 allotypic **antibodies**. The recombinant molecule consisting of **VH** and **light chain** from the homogeneous **antibody** is active in an antigen binding assay.

L39 ANSWER 38 OF 39 EMBASE

reserved on STN
ACCESSION NUMBER: 74021031 EMBASE
DOCUMENT NUMBER: 1974021031
TITLE: The aminoterminal sequence of **antibody light chains**: evidence for possible inheritance of structural genes.
AUTHOR: Braun D.G.; Jaton J.C.
CORPORATE SOURCE: Basel Inst. Immunol., Basel, Switzerland
SOURCE: Molecular Immunology, (1973) Vol. 10, No. 6, pp. 387-395.
CODEN: IMCHAZ
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
AB Amino terminal sequence analyses of 12 rabbit **antibody light chains** with restricted heterogeneity induced with either streptococcal group or pneumococcal type antigens are described. A comparison of their 27-30 N-terminal residue positions and comparison with the homologous regions of human and mouse kappa chains suggest the following conclusions: Rabbit, mouse and human kappa chains are homologous. They share the prototype N-terminal sequence Asp Ile Val Met Thr Gln and predominantly or exclusively a number of residues further on in the N-terminal 27 positions (e.g. Pro 9, Gly 17, Thr 21, Ile 22, **Cys** 24, Ala 26 and Ser 27). The prototype rabbit **light chain** sequence appears to start with Ala Asp Ile Val Met, and is thus longer by one residue than human and mouse kappa chains. Like their human and mouse counterparts rabbit kappa chains can be subgrouped. A minimum number of six subgroups is distinguishable on the basis of the current sequence information. The existence of species specific amino acid residues in the region reported appears to be doubtful because positions 12 and 18 are also found to be variable. Rabbit allotype b4 **light chains** show the greatest variations in the N-terminal 5 amino acid positions with the highest variability index in position 3. The degree of homology of **antibody light chain** N-termini appears to be a function of the breeding relationship of individual rabbits. For example, **antibody light chains** of a parent and an offspring rabbit with identical specificities were identical within their N-terminal 22 amino acid residues. These data would imply inheritance of structural v-region genes for the synthesis of specific anti **polysaccharide antibodies**.

L39 ANSWER 39 OF 39 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1972:45369 BIOSIS
DOCUMENT NUMBER: PREV197208045369; BR08:45369
TITLE: SEQUENCE OF **CYSTEINE** CONTAINING PEPTIDES FROM HOMOGENEOUS RABBIT **ANTIBODY LIGHT CHAINS**.
AUTHOR(S): FRASER K; STROSBERG A D; MARGOLIES M N; PERRY D; HABER E
SOURCE: Federation Proceedings, (1972) Vol. 31, No. 2, pp. 742.
CODEN: FEPRA7. ISSN: 0014-9446.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

FILE 'MEDLINE' ENTERED AT 12:44:24 ON 17 JAN 2006

Searcher : Shears 571-272-2528

FILE LAST UPDATED: 14 JAN 2006 (20060114/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

```
L40        64450 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES/CT
L41        21516 SEA FILE=MEDLINE ABB=ON  PLU=ON  CYSTEINE/CT
L42          105 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND L41
L43        29761 SEA FILE=MEDLINE ABB=ON  PLU=ON  POLYMERS/CT
L44            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND L43


L40        64450 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES/CT
L41        21516 SEA FILE=MEDLINE ABB=ON  PLU=ON  CYSTEINE/CT
L42          105 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND L41
L45            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  "GENES, IMMUNOGLOBULIN
                  LIGHT CHAIN"/CT
L46            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  "GENES, IMMUNOGLOBULIN
                  HEAVY CHAIN"/CT
L47            0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND (L45 OR L46)


L40        64450 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES/CT
L45            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  "GENES, IMMUNOGLOBULIN
                  LIGHT CHAIN"/CT
L46            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  "GENES, IMMUNOGLOBULIN
                  HEAVY CHAIN"/CT
L48            0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND (L45 OR L46)
```

L44 ANSWER 1 OF 1 MEDLINE on STN

ACCESSION NUMBER: 93041795 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1420204
TITLE: Antibody and peptide probes of interactions between the SH1-SH2 region of myosin subfragment 1 and actin's N-terminus.
AUTHOR: Cartoux L; Chen T; DasGupta G; Chase P B; Kushmerick M J; Reisler E
CORPORATE SOURCE: Department of Chemistry, University of California, Los Angeles 90024.
CONTRACT NUMBER: AR 22031 (NIAMS)
HL 31962 (NHLBI)
SOURCE: Biochemistry, (1992 Nov 10) 31 (44) 10929-35.
Journal code: 0370623. ISSN: 0006-2960.

Searcher : Shears 571-272-2528

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921208

ED Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921208

AB The negatively charged residues in the N-terminus of actin and the 697-707 region on myosin subfragment 1 (S-1), containing the reactive cysteines SH1 and SH2, are known to be important for actin-activated myosin ATPase activity. The relationship between these two sites was first examined by monitoring the rates of SH1 and SH2 modification with N-ethylmaleimide in the presence of actin and, secondly, by testing for direct binding of SH1 peptides to the N-terminal segment on actin. While actin alone protected SH1 from N-ethylmaleimide modification, this effect was abolished by an antibody against the seven N-terminal amino acids on actin, F(ab)(1-7), and was greatly reduced when the charge of acidic residues at actin's N-terminus was altered by carbodiimide coupling of ethylenediamine. Neither F(ab)(1-7) nor ethylenediamine treatment reversed the effect of F-actin on SH2 reactivity in SH1-modified S-1. These results show a communication between the SH1 region on S-1 and actin's N-terminus in the acto-S-1 complex. To test whether such a communication involves the binding of the SH1 site on S-1 to the N-terminal segment of actin, the SH1 peptide IRICRKG-NH2(4+) was used. Cosedimentation experiments revealed the binding of three to six peptides per actin monomer. Peptide binding to actin was affected slightly, if at all, by F(ab)(1-7). The antibody also did not change the polymerization of G-actin by the peptides. The peptides caused a small reduction in the binding of S-1 to actin and did not change the binding of F(ab)(1-7).(ABSTRACT TRUNCATED AT 250 WORDS)

L41 21516 SEA FILE=MEDLINE ABB=ON PLU=ON CYSTEINE/CT
L43 29761 SEA FILE=MEDLINE ABB=ON PLU=ON POLYMERS/CT
L49 4126 SEA FILE=MEDLINE ABB=ON PLU=ON "IMMUNOGLOBULIN FRAGMENTS"/CT
L50 53 SEA FILE=MEDLINE ABB=ON PLU=ON L49 AND L41
L51 1 SEA FILE=MEDLINE ABB=ON PLU=ON L50 AND L43

L52 1 L51 NOT L44

L52 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 75012538 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4213239
TITLE: Mechanism of immunoglobulin polymer assembly.
AUTHOR: Koshland M E; Wilde C E 3rd
SOURCE: Advances in experimental medicine and biology, (1974) 45 (0) 129-38.
Journal code: 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197412

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19741219

ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19741219

FILE 'HOME' ENTERED AT 12:48:45 ON 17 JAN 2006

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=> d his ful

     (FILE 'CAPLUS' ENTERED AT 11:59:01 ON 17 JAN 2006)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 12:06:45 ON 17 JAN 2006
               E POLYMETHYLENE/CN 5
               E POLYETHYLENE/CN 5
L1           1 SEA ABB=ON  PLU=ON  POLYETHYLENE/CN
               E POLYBUTYLENE/CN 5
L2           1 SEA ABB=ON  PLU=ON  POLYBUTYLENE/CN
               E POLYPROPYLENE/CN 5
L3           1 SEA ABB=ON  PLU=ON  POLYPROPYLENE/CN
               E POLYOXYMETHYLENE/CN 5
               E POLYOXYETHYLENE/CN 5
               E POLYOXYBUTYLENE/CN 5
               E POLYOXYPROPYLENE/CN 5
               E POLYETHYLENE GLYCOL/CN 5
L4           1 SEA ABB=ON  PLU=ON  "POLYETHYLENE GLYCOL"/CN
               E POLYPROPYLENE GLYCOL/CN 5
L5           1 SEA ABB=ON  PLU=ON  "POLYPROPYLENE GLYCOL"/CN
               E POLYVINYL ALCOHOL/CN 5
               E METHOXYPOLYETHYLENE GLYCOL/CN 5
               E "METHOXY(POLYETHYLENE GLYCOL)"/CN 5
               E "METHOXY (POLYETHYLENE GLYCOL)"/CN 5
L6           1 SEA ABB=ON  PLU=ON  9004-74-4/RN
               D CN
               E "METHOXYPOLY(ETHYLENE GLYCOL)"/CN 5
L7           1 SEA ABB=ON  PLU=ON  "METHOXYPOLY(ETHYLENE GLYCOL)"/CN
L8           6 SEA ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7


     FILE 'HCAPLUS' ENTERED AT 12:11:29 ON 17 JAN 2006
L9      461491 SEA ABB=ON  PLU=ON  L8 OR POLYALKYLENE OR POLYALKENYLENE
               OR POLYOXYALKYLENE OR POLY(W)(ALKYLENE OR ALKENYLENE OR
               OXYALKYLENE OR OXY ALKYLENE OR METHYLENE OR PROPYLENE OR
               ETHYLENE OR BUTYLENE) OR POLYOXY ALKYLENE
L10     505667 SEA ABB=ON  PLU=ON  POLY(W)(OXYMETHYLENE OR OXYETHYLENE OR
               OXYBUTYLENE OR OXYPROPYLENE) OR POLYOXYMETHYLENE OR
               POLYOXYETHYLENE OR POLYOXYBUTYLENE OR POLYOXYPROPYLENE OR
               POLYETHYLENE OR POLYBUTYLENE OR POLYMETHYLENE OR POLYETHYLE
               NE OR POLYSACCHARIDE OR POLY SACCHARIDE OR PEG
L11     235187 SEA ABB=ON  PLU=ON  POLYPROPYLENE OR (POLYVINYL OR POLY
               VINYL)(W)(ALC OR ALCOHOL) OR METHOXYPOLYETHYLENE
L12      12137 SEA ABB=ON  PLU=ON  (L9 OR L10 OR L11) AND ANTIBOD?
L13        387 SEA ABB=ON  PLU=ON  L12 AND (VL OR VH OR HEAVY OR LIGHT OR
               V(2W)(H OR L))(5A)CHAIN

     FILE 'REGISTRY' ENTERED AT 12:17:28 ON 17 JAN 2006
               E CYSTEINE/CN 5
L14          2 SEA ABB=ON  PLU=ON  CYSTEINE/CN


     FILE 'HCAPLUS' ENTERED AT 12:17:53 ON 17 JAN 2006
L15         30 SEA ABB=ON  PLU=ON  L13 AND (L14 OR CYS OR CYSTEIN##)
L16          2 SEA ABB=ON  PLU=ON  L15 AND CHAPMAN ?/AU
               D TI AU 1-2
               D KWIC
               D KWIC 2
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     FILE 'REGISTRY' ENTERED AT 12:20:17 ON 17 JAN 2006
                E POLYVINYL ALCOHOL/CN 5
                E "POLY(VINYL ALCOHOL)"/CN 5
L17           1 SEA ABB=ON  PLU=ON  "POLY(VINYL ALCOHOL)"/CN

     FILE 'HCAPLUS' ENTERED AT 12:21:02 ON 17 JAN 2006

L18       12264 SEA ABB=ON  PLU=ON  (L9 OR L10 OR L11 OR L17 OR PVA OR PPG
                OR MPEG) AND ANTIBOD?
L19         389 SEA ABB=ON  PLU=ON  L18 AND (VL OR VH OR HEAVY OR LIGHT OR
                V(2W)(H OR L))(5A)CHAIN
L20          30 SEA ABB=ON  PLU=ON  L19 AND (L14 OR CYS OR CYSTEIN##)
L21           2 SEA ABB=ON  PLU=ON  L20 AND CHAPMAN ?/AU
                D KWIC
                D KWIC 2
L22        8615 SEA ABB=ON  PLU=ON  (L9 OR L10 OR L11 OR L17 OR PVA OR PPG
                OR MPEG)(L)ANTIBOD?
L23         195 SEA ABB=ON  PLU=ON  L22(L)(VL OR VH OR HEAVY OR LIGHT OR
                V(2W)(H OR L))(5A)CHAIN
L24          12 SEA ABB=ON  PLU=ON  L23(L)(L14 OR CYS OR CYSTEIN##)
L25           1 SEA ABB=ON  PLU=ON  L24 AND CHAPMAN ?/AU
                D KWIC
                D AN
                D AN L16 2
L26           1 SEA ABB=ON  PLU=ON  1L6 AND (SULPHUR OR SULFUR)
                D KWIC
                D AN
L27           2 SEA ABB=ON  PLU=ON  L16 AND (LINK? OR CONJUGAT?)
                D KWIC 2
                D AN 2

     FILE 'REGISTRY' ENTERED AT 12:26:28 ON 17 JAN 2006
                E SULPHUR/CN 5
L28           1 SEA ABB=ON  PLU=ON  SULPHUR/CN

     FILE 'HCAPLUS' ENTERED AT 12:26:34 ON 17 JAN 2006
L29           3 SEA ABB=ON  PLU=ON  L20 AND (L28 OR SULPHUR OR SULFUR)
L30           2 SEA ABB=ON  PLU=ON  L29 AND CHAPMAN ?/AU
                D TI AU 1-2
                D KWIC 2
L31         227 SEA ABB=ON  PLU=ON  L18 AND (L14 OR CYS OR CYSTEIN##)
L32          10 SEA ABB=ON  PLU=ON  L31 AND (L28 OR SULFUR OR SULPHUR)

     FILE 'REGISTRY' ENTERED AT 12:28:29 ON 17 JAN 2006

     FILE 'HCAPLUS' ENTERED AT 12:28:29 ON 17 JAN 2006
                D QUE L29
                D QUE L32
L33          10 SEA ABB=ON  PLU=ON  L29 OR L32
                D 1-10 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO, RAPRA, PROMT, PASCAL, CBNB, CIN' ENTERED AT
     12:29:51 ON 17 JAN 2006

     FILE 'HCAPLUS' ENTERED AT 12:30:45 ON 17 JAN 2006
L34         137 SEA ABB=ON  PLU=ON  L31 AND (LINK? OR CONJUGAT?)
L35          17 SEA ABB=ON  PLU=ON  L20 AND (LINK? OR CONJUGAT?)
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Searcher : Shears 571-272-2528

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                D KWIC
L36           1 SEA ABB=ON  PLU=ON  L34 AND (MONOVALEN? OR MONO VALEN?)
L37           8 SEA ABB=ON  PLU=ON  L20 NOT (PY=>1996 OR PD=>19961210)

     FILE 'REGISTRY' ENTERED AT 12:40:02 ON 17 JAN 2006

     FILE 'HCAPLUS' ENTERED AT 12:40:02 ON 17 JAN 2006
                D QUE L37
                D L37 1-8 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO, RAPRA, PROMT, PASCAL, CBNB, CIN' ENTERED AT
     12:40:46 ON 17 JAN 2006
L38          47 SEA ABB=ON  PLU=ON  L20
L39          39 DUP REM L38 (8 DUPLICATES REMOVED)
                D 1-39 IBIB ABS

     FILE 'MEDLINE' ENTERED AT 12:44:24 ON 17 JAN 2006
                E ANTIBODIES/CT 5
L40       64450 SEA ABB=ON  PLU=ON  ANTIBODIES/CT
                E CYSTEINE/CT 5
L41       21516 SEA ABB=ON  PLU=ON  CYSTEINE/CT
L42         105 SEA ABB=ON  PLU=ON  L40 AND L41
                E POLYMERS/CT 5
L43       29761 SEA ABB=ON  PLU=ON  POLYMERS/CT
L44           1 SEA ABB=ON  PLU=ON  L42 AND L43
                E "GENES, IMMUNOGLOBULIN LIGHT CHAIN"/CT 5
L45           1 SEA ABB=ON  PLU=ON  "GENES, IMMUNOGLOBULIN LIGHT CHAIN"/CT

L46           1 SEA ABB=ON  PLU=ON  "GENES, IMMUNOGLOBULIN HEAVY CHAIN"/CT

L47           0 SEA ABB=ON  PLU=ON  L42 AND (L45 OR L46)
L48           0 SEA ABB=ON  PLU=ON  L40 AND (L45 OR L46)
                D QUE L44
                D QUE L47
                D QUE L48
                D L44 .BEVERLYMED

     FILE 'HOME' ENTERED AT 12:47:09 ON 17 JAN 2006

     FILE 'MEDLINE' ENTERED AT 12:48:05 ON 17 JAN 2006
                E IMMUNOGLOBULIN FRAGMENTS/CT 5
L49        4126 SEA ABB=ON  PLU=ON  "IMMUNOGLOBULIN FRAGMENTS"/CT
L50          53 SEA ABB=ON  PLU=ON  L49 AND L41

L51           1 SEA ABB=ON  PLU=ON  L50 AND L43
                D QUE
L52           1 SEA ABB=ON  PLU=ON  L51 NOT L44
                D .BEVERLYMED

     FILE 'HOME' ENTERED AT 12:48:45 ON 17 JAN 2006


     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   15 JAN 2006  HIGHEST RN 871978-73-3
     DICTIONARY FILE UPDATES:  15 JAN 2006  HIGHEST RN 871978-73-3

                    Searcher    :     Shears     571-272-2528
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMI for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 17 Jan 2006 VOL 144 ISS 4
FILE LAST UPDATED: 16 Jan 2006 (20060116/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 14 JAN 2006 (20060114/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 11 January 2006 (20060111/ED)

FILE EMBASE
FILE COVERS 1974 TO 12 Jan 2006 (20060112/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 16 JAN 2006 <20060116/UP>
MOST RECENT DERWENT UPDATE: 200604 <200604/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://scientific.thomson.com/support/products/dwpi/

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS:
http://scientific.thomson.com/support/products/dwpifv/

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:
http://scientific.thomson.com/support/patents/dwpiref/reftools/classif

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

Searcher : Shears 571-272-2528

FILE SCISEARCH

FILE COVERS 1974 TO 11 Jan 2006 (20060111/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 10 JAN 2006 (20060110/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 02 JAN 2006 <20060102/UP>
FILE COVERS APR 1973 TO SEPTEMBER 29, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE.
USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE
DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION
ABOUT THE IPC REFORM <<<

FILE RAPRA
FILE LAST UPDATED: 10 JAN 2006 <20060110/UP>
FILE COVERS 1972 TO DATE

>>> Simultaneous left and right truncation is available in the
basic index (/BI), and in the controlled term (/CT),
geographical term (/GT), and non-polymer term (/NPT) fields. <<<

>>> The RAPRA Classification Code is available as a PDF file
>>> and may be downloaded free-of-charge from:
>>> http://www.stn-international.de/stndatabases/details/rapra_classco

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE.
USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE
DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION
ABOUT THE IPC REFORM <<<

FILE PROMT
FILE COVERS 1978 TO 14 JAN 2006 (20060114/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE PASCAL
FILE LAST UPDATED: 16 JAN 2006 <20060116/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

FILE CBNB
FILE LAST UPDATED: 17 JAN 2006 <20060117/UP>
FILE COVERS 1984 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE
BASIC INDEX (/BI) AND IN THE CHEMICAL NAME (/CN) FIELDS <<<

FILE CIN

FILE COVERS 1974 - 12 JAN 2006 (20060112/ED) VOL 35 ISS 3

FILE HOME

Searcher : Shears 571-272-2528